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COLLOID GLANDS (GOITRES): THEIR ETIOLOGY AND PHYSIOLOGICAL SIGNIFICANCE.[1]

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Our object in this paper is to present certain data concerning the production, the anatomical and the physiological status of uncomplicated colloid glands (goitres). These observations have been made upon sheep's and dogs' thyroids, and though still incomplete, they tend to modify to some extent the generally held opinions as to the exact place in pathology which colloid glands should occupy.

Before taking up these data it may be well to mention briefly the great anatomical groupings that one has to deal with in establishing a point of departure for the study of the processes involved. These are four, viz: (1) Normal glands; (2) Colloid glands (goitres, all degrees); (3) Hyperplastic thyroids (all degrees); (4) Complications (engrafted on any of the three preceding groups). Barring *atrophies, neoplasms* and *infections,* all thyroids naturally fall into one or another of these four groups. Leaving out of consideration the last group (complications), for we are not concerned with them here, the anatomical characteristics of the remaining groups are well defined and generally known. (Johns Hopkins Hospital Bulletin, 1907, XVIII, 359.)

The literature dealing with colloid glands (goitres) is highly complicated, and for very sufficient reasons: First, it has dealt almost entirely with human material, and, as is well known, most operative specimens show one or more secondary changes (complications). It is due to this fact in particular that existing classifications of goitres include such terms as cystic, calcareous, fibrous, vascular, gelatinous, etc. These terms, it seems, should not be raised to primary importance since, as Virchow (Die krankhaften Geschwülste, III, 4) has pointed out, they are only examples of complications engrafted on a more fundamental type of change. Probably the essential reason why we do not find any very definite description of colloid glands (goitres) in the literature is because their comparative and experimental pathology has been but little developed and it is only in the lower animals that we are able to study uncomplicated forms in series.

In this discussion of colloid glands (goitres) we are using

[1] Presented in abstract at the meeting of the American Association of Pathologists and Bacteriologists, Ann Arbor, Mich., April 17, 1908.

the term "goitre" parenthetically for the following reasons: (1) In the older literature of human pathology other cervical enlargements than those of the thyroid have been described as goitre; (2) The term has been applied to a great variety of thyroid enlargements, viz: cysts, fœtal adenomata, malignant tumors and inflammatory swellings, etc.; (3) Goitre is primarily a clinical term; (4) There is a growing tendency, and rightly we think, to include under the term goitre the entire group of anatomical changes of which the major ones are those of the thyroid (hyperplasia) and lymphoid tissues (spleen, thymus and lymph glands). (Marie: Gaz. d. Hôp., 1893, 202; Hektoen: Internat. Med. Mag., 1895-6, IV, 584; Kocher: Arch. f. klin. Chir., 1908, LXXXVII, 131; Caro: Berl. klin. Wchnschr., 1907, XLIV, 519; Boit: Frankfurt. Ztschr. f. Path., Bd. I, 187; Hirschlaff: Deutsche Ztschr. f. klin. Med., 1899, XXXVI, 200; Hart: München. med. Wchnschr., 1908, LV, Nos. 13 and 14.)

Since thyroids frequently show quite marked degrees of hyperplasia without being noticeable clinically (the preclinical stage of goitre), and also since there may be distinct anatomical evidences of a previous active hyperplasia in a gland now rich in colloid, although the gland clinically or macroscopically is not enlarged, it might be confusing to use the word "goitre" unguardedly. Thus we include under the term colloid glands (goitres) all glands which show histological evidence of reversion from any degree of previous active hyperplasia irrespective of the size of the glands.

Brief mention has already been made in previous papers (Johns Hopkins Hospital Bulletin, 1907, XVIII, 359; Arch. of Int. Med., 1908, I, 349) of the incidence and nature of the anatomical changes that occur in thyroids undergoing active hyperplasia, one sequence of which is the production of colloid glands (goitres). We have called this change "reversion" because it seemed to us from the observed phenomena in animals that the changes were best interpreted as the return of the hyperplasia to a more normal type of gland.

The data which follow are presented somewhat in the order of their observation and will be discussed under the following headings: (1) Anatomical changes; (2) Age of the animals; (3) Inconstant changes following the removal of one lobe of the thyroid and the possibility of other factors than quantity of thyroid influencing thyroid changes; (4) More direct evidence of some additional factors determining thyroid hyperplasia, and reversion; (5) Effect of administration of iodin, the relation of iodin to gland structure, etc.; (6) Comparison of the general biological reactions of colloid and of normal glands; (7) The preventive effect of iodin on secondary hyperplasia; (8) Summary.

1. Anatomical Changes.

In the routine histological examination of seven hundred (700) dogs' thyroids several examples of colloid glands (goitres) were met with—some complicated, others in pure form. We also observed what appeared to us to be transitional forms, *i. e.*, forms partaking both of the characteristics of colloid glands (goitres) and of active hyperplasias. By arranging these in series with the pure colloids at one end, and the active hyperplasias at the other, the gradations could easily be traced step by step by means of certain common features. *First,* in all specimens there were infoldings and plications of the lining epithelium of the alveoli which in the pure colloid glands appeared as twigs covered with the flat cubical epithelium characteristic of that lining the alveolar walls proper. In the transitional forms these same infoldings and plications were covered with higher forms of epithelium ranging up to columnar, which also conformed to that of the ruling type of epithelial cells lining the alveolar walls proper. In the pure active hyperplasias the infoldings as well as the alveolar walls proper were always covered with columnar epithelium.

Secondly, the stainable colloid approaches nearest the normal type in the true colloid glands and gradually becomes paler, more vacuolated and granular as we pass through the transitional forms to the true active marked hyperplasias, where it is generally absent or nearly so.

Thirdly, the vascularity and condition of the vessels show distinct and graded changes from the comparatively very slightly vascular pure colloid glands up to the markedly vascular active hyperplasias, while the vessel walls in pure colloid glands show distinct obliterating endarteritis similar, histologically, to that occurring in the involuting uterus or thymus.

These gradations of anatomical changes in the epithelium, the colloid and the vessels are very striking in the dog where such a series of colloid glands is easily obtained (in goitrous districts).

2. Age of the Animals.

The factor of age is important. Our only series of thyroids in which sufficiently large numbers of naturally occurring colloid glands were found (dog and man) illustrate very strikingly that colloid glands occur in older animals while the active hyperplasias occur in younger animals. This has long been recognized however, and is implied in the commonly used term "colloid degeneration of" which also implies the existence of an earlier and different anatomical condition of the gland. This factor of age differences between colloid and hyperplastic glands is in itself evidence that, normally, colloid glands are derived from hyperplasias; but above all else it raises the question of whether this colloid change might not be interpreted as physiological as well as pathological.

In this connection some of our earlier experiments, undertaken to repeat Halsted's[1] work on compensatory hypertrophy of the thyroid, might be of value.

3. Changes Following the Removal of One Lobe.

As most of our dogs when admitted to the laboratory show some degree of active hyperplasia of the thyroid it occurred to us to remove but one lobe from each of a few animals and note

[1] Johns Hopkins Hosp. Rep., Balto., 1896, I, 373.

what occurred. All the lobes removed showed some degree of hyperplasia. The dogs were kept from 24 days to one year, and on examining the remaining lobe we found, instead of further hyperplasia in all, as expected, that in some cases the remaining lobe had reverted to the colloid state while in others the remaining lobe had undergone further hyperplasia. These observations are presented in the following tables:

TABLE Ia.

No. of dog; sex; age; weight.	Date of first operation.	Date of second operation.	Lobe removed; weight of (gms.)	Histological classification of lobe.	Iodin per gram dried.	Iodin per gram fresh.
D-99a. male, middle, 8.4 kg.	29-I-06		Rt.; 7.2	Early gland. hyperplasia.	Not de	term'd.
D-99b.		16 I 07	Lt.; 4.5	Colloid.	1.538	0.458
D-85a. male, middle, 15.9 kg.	17 I-06		Rt.; 5	Early gland. hyperplasia.	Not de	term'd.
D-85b.		11 I-07	Lt.; 3.85	Colloid.	2.784	0.812
D-130a. female, middle, 9.6 kg.	14-II-06		Rt.; 1.9	Mod. gland. hyperplasia.	Not de	term'd.
D-130b.		30-X-06	Lt.; 1.5	Early gland. hyperplasia.	"	"
D-131a. male, middle, 9.7 kg.	14-II-06		Rt.; 6.9	Mod. gland. hyperplasia.	"	"
D-131b.		27-V-06	Lt.; 6	Mod. gland. hyperplasia.	"	"
D-207a. male, middle, 5.4 kg.	6-XII-06		Rt.; 2.1	Mark'd gland. hyperplasia.	"	"
D-207b.		27-I-07	Lt.; 1.6	Colloid—early gland. hyperplasia.	"	"

TABLE Ib.

No. of dog; sex; age; weight.	Date of first operation.	Date of second operation.	Lobe removed; weight of (gms.)	Histological classification of lobe.	Iodin per gram dried.	Iodin per gram fresh.
D-100a. male, middle, 11.81 kg.	29-I-06		Rt.; 2.4	Mod. gland. hyperplasia.	Not de	term'd.
D-100b.		9-I-07	Lt.; 1.9	Mark'd gland. hyperplasia.	0.171	0.045
D-175a. male, puppy, 8.4 kg.	25 IV-06		Rt.; 1	Mod. gland. hyperplasia.	Not de	term'd.
D-175b. 13.2.		25-I-07	Lt.; 1.05	Mark'd gland. hyperplasia.	0.135	0.029
D-208a. male, middle.	11-XII-06		Rt.; 3	Mod. gland. hyperplasia.	Not de	term'd.
D-208b.		4-I-07	Lt.; 3.5	Mark'd gland. hyperplasia.	"	"

Table Ia includes those cases in which reversion occurred in the remaining lobe, and Table Ib those cases in which further hyperplasia occurred. All these animals were kept in the same kennel, subjected to the same conditions, and clinically were in excellent health at the time of killing.

At first glance these observations seemed to us only a confirmation of the well known fact brought out by Halsted, viz: That if sufficient gland is not removed there is no compensatory hyperplasia of the remaining portion. However, on closer study there seemed to be more than this. In one group there was a reversion to a more normal type of gland while in the other there was further hyperplasia. All showed slight active hyperplasia of the first lobe removed, but the individual differences were slight. All were kept under similar conditions as far as possible. There were not sufficient differences in the size of the glands of the two groups or of the age of the animals to be of noteworthy importance, and we were forced to conclude that other factors than the amount of thyroid were concerned, not only in those cases where reversion occurred but also in those in which further hyperplasia resulted. Here are seen opposite histologic changes under apparently constant conditions. Is one pathological and the other physiological? We are inclined to look upon both as physiological in the sense that they represent the result of nature's attempts at establishing a normal condition. On this basis those cases which showed further hyperplasia easily become physiological (compensatory hyperplasia), but those cases which showed a colloid change (reversion) cannot be interpreted as physiological unless we suppose the existence of another factor than quantity of thyroid—some substance normally needed by the animal and whose presence or absence also has an influence on the cellular activities of the gland.

4. Thyroid Hyperplasia and Reversion.

In the light of this possibility that other factors than quantity of gland determine whether a gland already actively hyperplastic is to revert to the colloid state or undergo further hyperplasia the following observation is important: In the past two years we have from time to time removed small pieces of thyroid for histologic examination and then kept the animals for further experiments as needed. Looking over our records we find eight such cases. All were goitrous dogs and kept under the same conditions. Histologically the pieces of thyroids removed showed degrees of hyperplasia ranging from "marked" to "early-moderate." At the second operation, ranging from twenty days to three months later, it was found that the thyroids in all eight had undergone histologic changes toward colloid glands, *i. e.*, reversion—some only slightly, while others showed the completed changes to colloid. The dogs were all kept under the same laboratory conditions and liberally fed on cooked meat and bread. The problem is why these dogs, during their street life, maintained progressive hyperplasias while during their laboratory careers their thyroids, without exception, tended to revert to colloid glands. Certainly one thing seemed established, that some factor still unknown was influencing these gland changes, and from the clinical standpoint favorably, since the animals all gained weight.

5. Effect of Administration of Iodin, etc.

It was at this stage that we began to study experimentally the effects of iodin on the thyroid, thinking that further insight might be had by very careful comparisons of the histological structure with the iodin content. At any rate the question of iodin as a factor in these changes must either be more definitely established or eliminated, since clinically it has long been recognized as a specific remedy in the disease, and the work of Baumann, Oswald, Roos, Weiss, Hunt and others has established not only its normal presence in the

thyroid but that it is of the greatest significance in the physiological activity of the thyroid substance. Our earlier experiments with feeding iodin have shown that coincident with the administration of iodin to dogs with active thyroid hyperplasias there occurs a return to the colloid state which histologically is identical with the spontaneously occurring colloid gland. This change in the dog is complete in from 20 to 30 days if small doses of some iodin-containing compound (0.5 cc. syr. ferrous iodid) are administered daily during the period. Since then we have undertaken experiments for tracing this process step by step during the administration of iodin. Thus we have removed every 5-7 days a piece of the gland sufficient for histological control and iodin determination with invariably the following result: That as the gland histologically changed to the colloid state there was a corresponding rise in the iodin content. A typical case may be reported in full.

Case A-119.—Male, black mongrel, aged 8 months, admitted April 6, 1908. General nutrition good, weight 8 kg. Thyroid lobes are symmetrically enlarged and appear about the size of hen's eggs. They are soft, compressible, with a definite expansile pulsation and a palpable thrill. There is a palpable isthmus.

April 10, 1908. Under ether anæsthesia a portion of the left lobe was removed, weighing 9.825 gm.

There was slight hæmorrhage. Moderate distension of the lymphatic trunks coursing over the gland. Operation lasted one hour. Dog made excellent recovery.

Gross Description of Portion of Gland Removed.—The capsule is slightly thickened, gland tissue soft, grey-red, very vascular, and no visible colloid.

Histological Diagnosis.—Marked glandular hyperplasia.

Iodin content per gm. dry = 0.200 mgm.
" " fresh = 0.040 "

April 10, '08, gave 10 gtt. syr. fer. iodid by mouth.
" 11, " " 30 " " " " " "
" 12, " " 40 " " " " " "
" 14, " " 40 " " " " " "

April 15, under ether anæsthesia, the remaining portion of the left lobe was removed, weight 20.5 gm. The dog withstood operation well.

Gross Description of the Portion Removed.—Similar to first portion as described above except that there is some visible colloid and slighter firmness in consistency.

Histological Diagnosis.—Colloid—moderate glandular hyperplasia.

Iodin per gm. dry = 2.861 mgm.
" " " fresh = 0.553 "

April 16. Dog in excellent condition, 40 gtt. syr. fer. iodid per mouth.

April 18. 100 gtt. syr. fer. iodid.

April 19. 100 gtt. syr. fer. iodid.

April 21. Bandages removed together with stitches. Healing per primam, 60 gtt. syr. fer. iodid.

April 22. Under ether anæsthesia a portion of the right lobe, weighing 1.5 gm., was removed. Immediately upon exposure of the gland it was noticeably different from the gland of previous operations in that it was much less vascular, firmer and translucent.

Gross Description of Portion Removed.—Capsule slightly thickened. Colloid is visible. Consistency moderately firm. Color is reddish-translucent.

Histological Diagnosis.—Colloid—moderate glandular hyperplasia.

Iodin per gm. dry = 4.078 mgm.
" " " fresh = 0.860 "

April 23. Dog in good condition. (From this time on no iodin was administered.)

April 24. No sign of infection, eats heartily.

April 26. Wound clean, healed.

April 28. Under ether anæsthesia a portion of the right lobe weighing 7.2 gm. was removed. Dog withstood operation well, no hæmorrhage. The remaining portion of the gland has notably decreased in size.

Gross Description of the Portion Removed.—Gland is firm, colloid abundant, capsule moderately thickened, vascularity noticeably lessened.

Histological Diagnosis.—Colloid—early glandular hyperplasia.

Iodin per gm. dry = 3.353 mgm.
" " " fresh = 0.749 "

April 30. Slight œdema of jaw; otherwise in good condition.

May 3. Slight diarrhœa, wound healed and bandage removed.

May 6. Under ether anæsthesia a portion of the remaining part of the right lobe, weighing 6.5 gm., was removed. Rapid recovery from operation.

Gross Description of Portion Removed.—The gland tissue is hard, clear, yellow in color, colloid abundant, very viscid, vascularity normal.

Histological Diagnosis.—Pure colloid gland (goitre).

Iodin per gm. dry = 3.522 mgm.
" " " fresh = 0.894 "

May 8. No swelling of jaw, no evidence of tetany; apparently both vocal cords paralyzed.

May 11. Wound healed per primam. Dog active, appetite excellent.

May 27. Condition excellent, fat, hair glossy.

June 1. Under ether anæsthesia a hurried examination failed to find the remaining part of right lobe, wound closed.

June 4. Stitches removed, wound healed.

June 15. Under ether anæsthesia the remaining portion of right lobe was found and part removed. After the operation had been completed the dog was killed by the careless administration of ether. An autopsy was immediately performed and the remainder of the right lobe, weighing 0.550 gm., was removed. There were two large accessory aortic thyroids, together weighing 0.750 gm. Their gross characteristics are the same as the portion of the thyroid lobe proper. Spleen and thymus slightly enlarged. Otherwise all the other organs were perfectly normal, both gross and microscopically. Weight of dog, 11.9 kg.

Gross Description of Thyroid Removed at Autopsy.—Colloid abundant, color clear yellow, firm to the touch, and of normal vascularity.

Histological Diagnosis.—Pure colloid gland (goitre).

Iodin per gm. dry = 2.770 mgm.
" " " fresh = 0.554 "

Summary.—The dog was under observation from April 6, 1908, to June 15, 1908—70 days, during which time six operations were performed consisting of the successive removals of portions of the thyroid and accompanied by the administration of moderate doses of syr. fer. iod. for a period of 12 days following the first operation. After this the dog got no iodin except what might have been obtained from a liberal diet consisting of cooked meat, bread, water and milk. Ar-

ranging the iodin contents and histological diagnoses of the portions of thyroid in the order of their removal, we have:

	Histological Diagnosis.	Iodin per gm. fresh, mgm.	Iodin per gm. dried, mgm.
1st operation.	Marked glandular hyperplasia	0.040	0.200
2d "	Colloid—moderate-marked ..	0.553	2.861
3d "	Colloid—moderate	0.860	4.078
4th "	Colloid—early	0.749	3.353
5th "	Pure colloid	0.894	3.522
6th "	Pure colloid	0.554	2.770

This case illustrates the rapidity with which iodin is taken up by the hyperplastic thyroid and the rapidity of the process of reversion as well. The dog grew rapidly, gaining in the 70 days 4.9 kg.

As the histologic appearances of the spontaneously occurring colloid glands are identical with those artificially produced by administration of iodin, and since the histologic characteristics of colloid glands so closely resemble those of the normal glands, it becomes of interest to compare the iodin contents of normal and of spontaneously produced colloid glands. It suffices here to state that such comparisons have been made, and they show that the iodin contents of these two groups are practically parallel, and that the iodin contents of colloids are also the nearest approach to those of normal glands with which one meets. Indeed they may equal those of normal glands.

Thus far we have considered anatomical and chemical characteristics of colloid glands, both those artificially produced and the spontaneously occurring ones, and have compared the findings with those of normal glands. In a sentence, it was found that colloid glands, both as regards their histological characteristics and iodin contents, were the nearest approach to the normal gland that is possible for actively hyperplastic thyroids.

6. Comparison of Biological Reactions of Colloid and Normal Glands.

Next in order, we undertook studies of the *biological characteristics* of colloid glands as compared with those known to be true of normal glands. First, we took colloid glands, and from time to time removed parts in the attempt to produce compensatory hyperplasia of the remaining part, just as occurs in the similar treatment of normal glands. The following case is illustrative:

Case A-106.—Middle-aged female, white, bull-terrier. Admitted June 1, 1907, in excellent condition, weight 11.8 kg. Physical examination revealed symmetrical enlargement of both thyroid lobes, each lobe roughly measuring 5x3.5 cm. Definite isthmus palpable. Lobes firm, hard and quite freely movable. Clinical diagnosis of pure colloid goitre was made on basis of excellent general condition and the firm, hard, non-pulsating lobes of thyroid.

June 5, 1907. Under ether anæsthesia right lobe was removed, weight 29.5 gm.

Gross Description.—Capsule 1 mm. thick, of dense white fibrous tissue. Gland tissue on section is clear brownish-yellow (old hæmorrhages), with abundant colloid, white fibrous trabeculæ are prominent throughout. Specimen saved for iodin determination and histological examination.

Histological Diagnosis.—Pure colloid gland (goitre).

Iodin per gm. dry = 0.308 mgm.
" " " fresh = 0.033 "

June 18, 1907. Wound healed per primam, bandage removed, dog in excellent condition, appetite good.

July 15, 1907. Under ether anæsthesia about one-half of the remaining left lobe was removed, weight 15 gm.

Gross Description of Part Removed.—Capsule thick, color and colloid much the same as the previous portion of the gland.

Histological Diagnosis.—Pure colloid gland (goitre).

Iodin per gm. dry = 0.554 mgm.
" " " fresh = 0.066 "

August 15, 1907. Dog in fair condition, wound healed, weight 9.52 kg.

September 10, 1907. Under ether anæsthesia about one-half of remaining half of left lobe removed, weight 3 gm. Specimen saved for iodin and histological examination.

Gross Description.—Quite vascular, bright red, moderately firm, some visibly dilated lymphatic trunks, some visible colloid.

Histological Diagnosis.—Colloid—moderate glandular hyperplasia.

Iodin per gm. dry = 0.554 mgm.
" " " fresh = 0.099 "

September 20, 1907. Dog in fair condition, wound healed.

December 7, 1907. Under ether anæsthesia remaining portion of left lobe was removed (as nearly as possible, since fibrous adhesions made it practically impossible to remove all traces of lobe).

Gross Description of Portion Removed.—Weight 4.5 gm., color bright red, soft, visible fibrous trabeculæ, capsule much thickened, quite vascular, some visible colloid.

Histological Diagnosis.—Marked glandular hyperplasia.

Iodin per gm. dry = 0.115 mgm.
" " " fresh = 0.022 "

December 11, 1907. Dog has ravenous appetite. On removing bandage slight skin infection noted, washed with HgCl, and dressed.

December 22, 1907. Wound healed. Dog still has ravenous appetite; given sulphur bath on account of beginning mange.

January 4, 1908. Dog very weak, emaciated, weight 9.1 kg., slight diarrhœa, with visible cardiac impulse that shook the dog. Dog has showed no signs of tetany. As the dog was rapidly becoming weaker, in spite of its good appetite, it was decided to administer small doses of iodin in the form of syr. fer. iod.; beginning January 4, 10 gtt. daily was given. At first the dog seemed to improve, and between January 4 and 18 gained 2.3 kg.

January 21, 1908. Dog died suddenly this afternoon; was not seen at time of death. Autopsy (probably one hour after death) showed that the increased weight was due to œdema of the fatty tissues. Both thyroid lobes were absent. The heart was enlarged and dilated, especially the right side. Pulmonary congestion and œdema. Stomach, liver, kidneys, brain and pituitary body normal in their gross appearances. There was quite a large mass of thymus tissue in the sub-sternal fat, and also two accessory thyroids. These two accessory thyroids weighed 0.95 gm. In their gross appearance they were soft, greyish-red and vascular.

Histological examination of the accessory thyroids showed a moderate glandular hyperplasia.

Iodin per gm. dry = 0.410 mgm.
" " " fresh = 0.095 "

A histological examination and iodin determination were made on the thymus gland with the following result:

Histological examination revealed the presence of numerous duct-like spaces lined by columnar epithelium, and containing desquamated epithelial cells and a pink staining albuminous material (a condition common to about 20 per cent of the dogs in this locality). One accessory parathyroid was found in the thymus upon histological examination.

Iodin per gm. dry = 0.018 mgm.
" " " fresh = 0.006 "

Summary.—Dog was under observation from June 1, 1906, to January 21, 1907, practically seven months. During this time parts of the thyroid were removed on four different occasions. The first and second specimens were histologically pure colloid, while the third and fourth specimens removed showed, respectively, colloid with moderate, and colloid with marked glandular hyperplasia.

The iodin determinations of these four specimens showed, roughly, a decrease in the iodin content, proportional to the degree of hyperplasia. The accessory thyroids, removed postmortem, while showing histologically a moderate glandular hyperplasia, showed a noticeable increase in their iodin contents over the last operative specimen. This was probably due, as was also the presence of iodin in the thymus, to the feeding of iodin during the last two weeks of life. The presence of iodin in the thymus was not due to the presence of accessory thyroids, a possibility suggested by Cunningham and Mendel (Am. J. Physiol., 1900, III, 285). The noteworthy increase in body-weight during the last three weeks might be interpreted as of myxœdematous origin, although there is no positive anatomical basis for such an opinion, even though both thyroid lobes had been removed.

In this case it is clearly seen that a compensatory change occurred following partial excision. The change is identical with that which occurs in the normal gland, and has been admirably described by Halsted, *i. e.*, the flattened cubical cells lining the enlarged alveoli increase in size, first cubical, then low columnar, then high columnar, together with a lessening and finally a disappearance of the stainable colloid, and at the same time a marked increase in vascularity. The change is as a rule not quite uniform as some alveoli contain densely staining colloid and flattened epithelium, while all the surrounding alveoli have undergone true hypertrophy.

Thus it seems highly probable that colloid glands react like normal glands in the experiments of their partial removal.

7. Preventive Effect of Iodin in Secondary Hyperplasia.

Continuing along this line of biological experiments, it is known that the administration of iodin will prevent the occurrence of compensatory hyperplasia following partial excision in normal glands which otherwise would hypertrophy. The following cases are illustrative of what occurs in the normal glands.

Case A-26.—Female puppy, age three months, admitted February 10, 1907, weight 2.4 kg., in fair condition, no palpable thyroids.

February 15, 1907. Under ether anæsthesia, right lobe removed, weight 0.24 gm.

Gross Description.—Capsule thin, delicate, color reddish-translucent, visible colloid normal, firm consistency.

Histological Diagnosis.—Normal thyroid.

Iodin per gm. dry = 2.300 mgm.
" " " fresh = 0.380 "

February 19, 1907. Dog in excellent condition, wound healed, bandage removed, weight 2.4 kg.

February 21, 1907. Beginning to-day 1 gtt. saturated alcoholic solution of iodin was daily administered with its ration, for 15 days, ending March 8, 1907. From this date on no iodin was given.

March 20, 1907. Dog growing rapidly, clinically in excellent condition.

April 2, 1907. Killed with chloroform this morning, weight 4 kg.

At autopsy remaining lobe (right) weighed 0.305 gm., color clear, reddish-yellow, colloid abundant, gland tissue firm, capsule thin and delicate.

Histological Diagnosis.—Normal thyroid.

Iodin per gm. dry = 3.467 mgm.
" " " fresh = 0.705 "

The fat deposits were normal. Spleen, kidneys, liver, lungs, heart and brain were normal in gross appearance.

Case T-25.—Female pup, aged 112 days, weight 1.8 kg., excellent condition (reared in laboratory).

September 6, 1907. Operated upon and the left lobe removed. Weight 0.350 gm. Normal in gross appearance, and also upon microscopic examination. No iodin determination.

September 11. Wound healed, bandage removed.

October 30. Weight 2.6 kg., excellent condition, killed by another dog. Right lobe removed and at autopsy weighed 0.355 gm.

Gross Appearance.—Soft, vascular.

Microscopic Diagnosis.—Moderate glandular hyperplasia. No iodin determination.

This case (T-25) illustrates what usually occurs in young dogs with normal glands following the removal of one lobe, viz: compensatory hyperplasia of the remaining lobe; and Case A-26 shows that this compensatory hyperplasia may be prevented by the administration of iodin although the thyroid increases in size in proportion to body weight. These cases, with many other similar experiments, also suggest that hyperplasia accompanied by a disappearance of the colloid and a change to columnar epithelium is not a part of the normal growth of a normal gland.

While we have no separate experiments on colloid glands to parallel the above cases, there have occurred several cases which indicate the same to be true for colloids, viz: That in the presence of full amounts of iodin smaller amounts of colloid gland suffice to supply the animal's needs. This being true it is obvious that by withholding iodin the hypertrophic changes may be hastened. At first a diet as free from iodin as possible was considered, and indeed attempted, but it is fraught with so many difficulties (well stated by Dochez, Johns Hopkins Hospital Bulletin, 1908, XIX, 235), chief among which is that we may be depriving the animal of other substances necessary to its normal economy in the attempt to eliminate iodin, that we chose merely to use a raw meat diet (beef). As will be brought out more fully in a later publica-

tion the restricting of iodin does hasten the occurrence of hypertrophy both in normal and in colloid glands.

The following case, since it combines several of the points just mentioned, may be reported in full:

CASE A-121.—Male, middle-aged fox-terrier, good condition, weight 7.3 kg. Admitted April 20, 1908. Thyroid lobes are symmetrically enlarged, joined by a palpable isthmus and roughly measuring 5x2.5 cm. The consistency is moderately firm; there is a definite, though slight, expansile pulsation; no thrill.

April 22, 1908. Under ether anæsthesia a part of the right lobe, weighing 4.6 gm., was removed. Dog withstood operation well.

Gross Description of Specimen Removed.—The capsule is somewhat thickened; vessels distinctly enlarged, color yellowish-opaque, consistency moderately firm and colloid is barely visible, as are the whitish ring-like outlines of the enlarged alveoli.

Histological Diagnosis.—Colloid—moderate glandular hyperplasia.

Iodin per gm. dry = 0.269 mgm.
" " " fresh = 0.059 "

April 24, 1908. Dog is in excellent condition.

April 26, 1908. Bandage removed, no evidence of infection. Dog does not seem quite normal, appetite poor.

April 28. Under ether anæsthesia another portion of the right lobe, weighing 7.6 gm., was removed. Excellent recovery.

Gross Description.—Same as first specimen.

Histological Diagnosis.—Colloid—moderate glandular hyperplasia.

Iodin per gm. dry = 0.455 mgm.
" " " fresh = 0.099 "

April 30, 1908. Slight œdema of jaw, appetite good.

May 8, 1908. Wound healed, dog in perfect health.

May 9, 1908. Under ether anæsthesia the remaining portion of the right lobe was removed, weighing 6.4 gm. Excellent recovery.

Gross Description.—Gland much firmer than previous specimens, has a distinct yellowish translucent appearance and more visible colloid, vascularity still above normal. The enlarged alveoli are more distinct.

Histological Diagnosis.—Colloid — early moderate glandular hyperplasia.

Iodin per gm. dry = 0.692 mgm.
" " " fresh = 0.167 "

May 11, 1908. Wound in good condition, dog has good appetite.

May 20, 1908. Wound perfectly healed.

May 21, 1908. Under ether anæsthesia a portion of the left lobe, weighing 3.6 gm., was removed. Dog made excellent recovery.

Gross Description.—There are scattered areas of brown pigmentation (old hæmorrhage), colloid normal, vascularity still slightly above normal. The enlarged alveoli are more distinct.

Histological Diagnosis.—Colloid—early glandular hyperplasia.

Iodin per gm. dry = 1.838 mgm.
" " " fresh = 0.520 "

May 27, 1908. Dog in excellent condition, wound healed.

June 2, 1908. Under ether anæsthesia another portion of the left lobe, weighing 1.2 gm., was removed. Large quantities of ether had to be used, and there was excessive bronchial secretion, otherwise the dog withstood the operation well.

Gross Description.—Colloid abundant, color clear, yellow, translucent, tissue firm, vascularity normal.

Histological Diagnosis.—Colloid—early glandular hyperplasia.

Iodin per gm. dry = 1.774 mgm.
" " " fresh = 0.446 "

June 3. Dog in good condition.

June 8. Bandage had slipped and dog had scratched skin wound open, wound granulating, no pus.

June 12. Wound healed. Under ether anæsthesia another portion, weighing 4.85 gm., was removed. Dog made excellent recovery. Large quantities of ether necessary.

Gross Description.—Colloid abundant, yellow, translucent in color, tissue firm, normal vascularity.

Histological Diagnosis.—Colloid—early glandular hyperplasia.

Iodin per gm. dry = 1.427 mgm.
" " " fresh = 0.369 "

June 16. Wound healed, stitches removed, dog in excellent condition.

June 27. Under ether anæsthesia removed another portion of the left lobe, weighing 4.2 gm. Dog made good recovery, some difficulty was encountered with mucus.

Gross Description.—Colloid abundant, color translucent yellow, tissue firm, vascularity normal. Outline of enlarged alveoli distinct.

Histological Diagnosis.—Pure colloid gland (goitre).

Iodin per gm. dry = 2.170 mgm.
" " " fresh = 0.550 "

July 2. Stitches removed, wound healed.

July 3. Mange suspected on account of some cutaneous irritation. An ointment of sulphur and lard was applied.

July 10. Dog in excellent condition. Under ether anæsthesia another portion of the left lobe, weighing 2 gm., was removed. Dog made excellent recovery from operation.

Gross Description.—Gland similar to last specimen described.

Histological Diagnosis.—Colloid—early glandular hyperplasia.

Iodin per gm. dry = 1.091 mgm.
" " " fresh = 0.188 "

July 11. A prophylactic dose of 1 cc. of a 5 per cent solution of calcium chloride was given with food, although there was no evidence of tetany.

July 14. Calcium chloride stopped. Dog in excellent condition.

July 18. Wound healed. Dog in excellent condition.

September 1. Dog in excellent condition, has gained in weight, now weighs 9.5 kg.

September 13. Under ether anæsthesia another portion of the left lobe was removed, weight 0.5 gm. Aside from large amount of ether necessary, and excessive bronchial secretion, dog withstood operation well.

Gross Diagnosis.—Tissue more vascular than in previous specimen, visible colloid distinctly less. The cut surface shows fine greyish trabeculæ, giving the specimen a distinct opacity.

Histological Diagnosis.—Colloid—early glandular hyperplasia.

Iodin per gm. dry = 1.082 mgm.
" " " fresh = 0.206 "

September 15. Dog in excellent condition; used sulphur ointment again.

September 19. Wound healed, stitches removed.

October 3. Dog apparently normal, given 20 gtt. syr. fer. iod. by mouth.

October 25. Finished the course of 15 cc. syr. fer. iod. by mouth.

November 1. Under ether anæsthesia a part of the remaining portion of the left lobe was removed, weighing 0.8 gm. The

scar tissue was moderately dense about it, but no difficulty was met with and dog rallied quickly from operation.

Gross Description of Specimen Removed.—Scar tissue at one edge is quite vascular, color of gland is clear, reddish-translucent, consistency firm, colloid normal. The alveoli are distinct.

Histological Diagnosis.—Pure colloid gland (goitre).

Iodin per gm. dry = 1.925 mgm.
" " " fresh = 0.513 "

November 2. As the operation injury to the tissue approached very near to the upper pole, and hence there was danger of having injured the presumably only remaining parathyroid, it was deemed advisable to give 10 cc. of a 5 per cent solution of calcium chloride as a prophylaxis.

November 4. 10 cc. of calcium chloride given; no evidence of tetany.

November 5. Wound healed. Stitches removed.

November 17. Dog very fat, weight 12.1 kg., active and alert.

December 21. Dog in excellent condition.

December 22. Under ether anæsthesia a part of the remaining portion of the left lobe was removed, weighing 0.355 gm.

Gross Description.—Color brownish-red, colloid visible, though reduced, vascular.

Histological Diagnosis.—Colloid—early glandular hyperplasia.

Iodin per gm. dry = 1.540 mgm.
" " " fresh = 0.305 "

December 26. Wound healed, stitches and bandage removed. Calcium chloride stopped. Weight, 12 kg.

In this case at the time of admission the thyroid was classified as colloid—moderate glandular hyperplasia, in which the histological picture was that of a spontaneous slow reversion from an active hyperplasia rather than that of a colloid gland undergoing further hyperplasia. We have summarized the experiment in the following tabulation:

SUMMARY.

Date of Operation.	Histological Diagnosis.	Iodin per gm. dry, mgm.	Iodin per gm. fresh, mgm.
April 22, '08.	Colloid—moderate glandular hyperplasia	0.269	0.059
April 28, '08.	Colloid—moderate glandular hyperplasia	0.455	0.099
May 9, '08.	Colloid—early glandular hyperplasia	0.692	0.167
May 21, '08.	Colloid—early glandular hyperplasia	1.838	0.520
June 2, '08.	Colloid—early glandular hyperplasia	1.774	0.446
June 12, '08.	Colloid—early glandular hyperplasia	1.427	0.369
June 27, '08.	Pure colloid gland	2.170	0.550
July 10, '08.	Colloid—early glandular hyperplasia	1.091	0.188
Sept. 13, '08.	Colloid—early glandular hyperplasia	1.082	0.206
Nov. 1, '08.	Pure colloid gland	1.925	0.513
Dec. 22, '08.	Colloid—early glandular hyperplasia	1.540	0.305

Thus, in a single experiment, starting with active hyperplasia we have followed the process back to colloid; to hyperplasia again; back to colloid, and finally to hyperplasia for the second time.

8. Summary and Discussion.

In the observations above recorded the following points were brought out:

(1) Colloid glands are in all their anatomical characteristics the nearest approach to normal glands that active hyperplasias can become.

(2) There are as many degrees and sizes of colloid glands as there are degrees and sizes of actively hyperplastic glands.

(3) There are all gradations from colloid glands to active hyperplasias.

(4) The iodin contents of colloid glands are the nearest approach to those of normal glands that it is possible for glands to attain to, which have once been the seats of active hyperplasia.

(5) Spontaneously occurring colloid glands are most frequently found in the well nourished and middle-aged animals.

(6) Colloid glands are known to occur from spontaneous reversion of hyperplasias or following the administration of iodin-containing substances to animals with hyperplasia, and in either case the resulting condition (colloid) is histologically the same.

(7) Partial removal of colloid glands is followed by the same compensatory hyperplasia as occurs in normal glands following their partial removal.

(8) The administration of iodin-containing substances will prevent the occurrence of secondary hyperplasia in colloid glands to the same extent that it prevents the occurrence of hyperplasia in normal glands following partial removal.

(9) It is possible by means of partial removals together with withholding and giving iodin to follow the process of reversion to a colloid gland; the process of compensatory hyperplasia, and the second process of secondary reversion in the same dog.

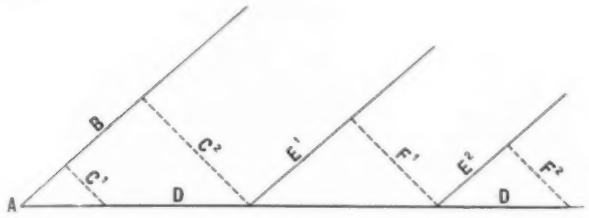
Thus it is seen that colloid glands as regards their *anatomical, chemical* and *general biological* characteristics obey all the laws of normal glands in so far as these laws are at present known.

These observations offer a rational explanation for the long known and ill understood phenomena of a goitre presenting some of the characteristics both of a colloid and of a hyperplasia (parenchymatous goitre) or of a hyperplasia occurring on a colloid basis, since it is possible to produce experimentally a hyperplasia on a colloid gland basis in just the same way as one produces a hyperplasia on a normal gland basis.

To illustrate the above fact from goitre in man, where such cases have been more frequently observed, this is what occurs in those cases recorded in the literature as "Secondary Graves' disease" or Graves' disease engrafted on an old colloid goitre in contrast with the so-called "Primary Graves' disease," which is the same process occurring on the basis of a normal gland. Then too the long life of man and a more careful study of goitre in man has allowed Lawson Tait (Edinb. M. J., 1875, XX, 993) to observe the "stair-step" like progress of goitre associated with multiple pregnancies. This process interpreted by our present standards would mean a hyper-

plasia during the pregnancies with reversion to colloid gland during the intervals, with each succeeding reversion not returning to the size of the preceding reversion.

This relationship of hyperplasias to colloid glands and to normal glands may be best presented in the following diagram:



A, normal gland; *B*, all degrees of primary hyperplasia occurring on the basis of a normal gland; *C*-1, 2, the several degrees of hyperplasia returning to colloid state; *D*, colloid glands; *E*-1, 2, etc., the several degrees of secondary hyperplasia engrafted on the basis of a colloid gland; *F*-1, 2, etc., the secondary reversion of the secondary hyperplasias. Thus one might have tertiary hyperplasias and reversions, etc.

These data, *anatomical, chemical* and *biological*, we believe are sufficient to justify the conclusion that in dogs and sheep, at least, all pure colloid glands are reversions from degrees of active hyperplasia and are the nearest approach to the normal quiescent condition that glands can ever assume which have once undergone active hyperplasia. Further, this return to the colloid state is nature's evidence of a relief from some physiological deficiency. Lastly, the process of reversion being *physiological* rather than *pathological*, it seems to us to be more closely allied with the *involution type of atrophy* than with *degeneration*.

We are indebted to Profs. Stewart, Howard and Sollmann for their careful criticisms.

LESIONS OF THE NERVE CELL AND VASCULAR TISSUES PRODUCED BY ACUTE EXPERIMENTAL ALCOHOLIC POISONING.*

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The effect of ethyl alcohol, in its pure form, upon the organism differs in some ways from that of spirituous liquors of which it is the chief constituent, doubtless from the fact that certain ethers are present in the spirits and absent from the alcohol. The first result, after the ingestion of a moderate quantity of ethyl alcohol in man—a fluid ounce, for example, of absolute alcohol properly diluted—is to cause a fall in the heart's action of from fifteen to twenty beats a minute, accompanied by some hardening of the quality of the pulse. This is followed, almost immediately, by a feeling of muscular lassitude, then of mental confusion, both of which increase gradually, but are lost in an hour or two.

A few instances of its more continued effects may be cited. One man of forty years, who voluntarily subjected himself for a month to a course of ethyl alcohol, in daily doses, beginning with two ounces and gradually increasing to four ounces, taken mainly in the late evening, exhibited the following symptoms: After the initial vascular disturbance came considerable mental confusion, inability to control the voluntary muscles, and intense sleepiness. On the following morning, after a period of from six to seven hours' profound sleep, there was considerable irritability of the heart's action, which persisted up to three or four o'clock the following afternoon, mental lassitude, and difficulty in keeping up with the daily routine work. By the end of the month there were well-marked and persistent irritability of the heart's action, palpitation, at times a feeling of præcordial anxiety with some difficulty in respiration, a pulse showing a considerable increase in tension, and decided evidence of dilatation of the peripheral arteries—all indications of beginning fatty changes in the heart and muscularis of the blood-vessels. With these symptoms were others indicating considerable digestive disturbance in the form of mucous diarrhœas, neuralgic pains in the forehead and limbs, together with a lessened ability to think clearly at any time, and mental irritability. When the alcohol was stopped, all the symptoms, including the arterial dilatation receded rapidly, and soon disappeared.

A second individual, who drank 95 per cent. alcohol as a beverage in the place of whiskey, to the extent of a pint or more a day, at the end of three months exhibited profound mental changes in the form of pronounced loss of memory for recent events, delusions of persecution, and on the somatic side, profound cutaneous anesthesias with loss of knee-jerks and other deep reflexes, also indications of a fatty heart muscle and dilated arteries. Tremor, loss of tone of the musculature, difficulty in articulation, incoordination of the voluntary movements, as well as lancinating pains in the lower extremities were also noted. He recovered, almost completely, after a three months sojourn at a sanitarium.

In a third individual—a physician—who consumed a litre bottle of absolute alcohol a day for a period of three months, the changes were more profound. The heart's action grew weak, weaker and more irregular, complete anesthesia of the skin surfaces with entire loss of the deep and superficial reflexes supervened. With these came various visceral paræsthesias; then a rapid dementia began, which soon became profound, and shortly after the end of the period of three months he died from failure of the heart's action.

The ingestion of large quantities of ethyl alcohol is always followed by profound disorganization of the cardiac func-

* Abstract Paper.

tions, and a single dose of six or eight ounces, may be followed by rapid death, even in persons who are accustomed to the habitual use of spirits. In these instances there is a gradual lowering of the circulation, sub-normal temperature, bluing of the extremities, and a gradual slacking of the cardiac action until the exitus.

The minute pathological effects of acute alcoholic poisoning upon the human organism is practically unknown, nor is it possible to obtain material for microscopic examinations in sufficiently fresh condition from cases of delirium tremens that have died as a result of their debauches, as from the tissues of the lower animals that have been subjected to practically the same course of treatment. We have, therefore, availed ourselves of the material, furnished during the course of certain studies by Dr. Julius Friedenwald, upon the effects of alcohol on the tissues of rabbits. The alcohol was administered in slowly increasing doses until the animal had established a certain tolerance of the drug; it was then increased to a considerable amount, which was maintained until the animal died.

While the quantity given the animals was large, it can hardly be said to exceed the amount taken by many men while on a protracted debauch, and from which they eventually recover, perhaps after an attack of delirium tremens or other alcoholic psychosis, and fell considerably below that of the man, cited above, who took a litre a day.

Thus an individual weighing 150 pounds would take in the same proportion fifty times the quantity of alcohol as a three pound rabbit, and accordingly would attain a daily allowance of 750 cc. absolute alcohol, equal to about 1500 cc. of ordinary whiskey, with the difference that the ethyl alcohol is perhaps less deleterious to the tissues than the blended whiskeys of commerce.

Three rabbits were used in this study:

Rabbit A, weighing 1220 grams, received 5 cc. diluted alcohol on September 26, and the amount was gradually increased up to 15 cc. a day, which was maintained until October 21, the date of death. In all he received 190 cc. alcohol. After the exitus the body weighed 780 grams, and at the autopsy the principal microscopic lesion was a fatty degeneration of the heart muscle.

Rabbit B, weighed 1500 grams on September 30, and from that date received a daily allowance of from 5 to 15 cc. alcohol, and died on October 21, at which time he weighed 840 grams; in this case also the chief demonstrable lesion was a fatty heart. The total amount of alcohol consumed by this rabbit was 165 cc.

Rabbit C, weighed 1490 grams. The administration of the drug in the same quantities was begun on October 2, and death resulted on October 25, by which time the weight had been reduced to 920 grams. This animal died in convulsions after having received a total of 260 cc. alcohol. A fatty heart was again found.

One point of considerable interest to be noted in this experiment is that the resistance of the several animals to the poison is not proportionate to their weight, but to some inherent property in their tissues; thus, the heaviest one received only 165 cc., and the next heaviest, weighing 10 grams less received 260 cc. before death resulted. In all the nutrition of the rabbits was kept up as well as possible by giving them suitable and attractive food.

Histological Examination.

The tissues derived from the three rabbit brains were hardened in absolute alcohol and in Müller's fluid, while the staining for microscopic examination was done by the Nissl method, various nuclear dyes, and the silver phospho-molybdate procedure.

The results are separable into three divisions according to the various elements involved, which may be briefly given as:

Blood-vessels.—Damage positive.

Nerve Cells.—Damage positive, yet not so profound as in the cells of the blood channel walls.

Neuroglia.—Damage positive as to the lymphoidal elements, negative for the suport neuroglia.

We will consider in their order these various pathological changes.

The Blood-Vessels With Nuclear Stains.

Arteries and Intermediary Vessels.—The nuclei of the endothelial cells are everywhere swollen, in places are fragmented, and receive either too little or too much of the dye. The cellular protoplasm is also undergoing definite retrogressive alterations. The cells of the intermediary vessels look as if they had been subjected to severe strain (dilatation of the blood-vessel), as their even contours are distorted, and there are many irregular bulges in the walls.

The changes in the muscular layer are equally interesting. Nuclei are here and there absent over considerable areas of the middle wall of the vessel, and in those that remain certain abnormalities are apparent, the nucleus being badly stained, either wholly or in part. It is, however, in the substance of the muscular protoplasm that the lesions are most apparent, and show that the cells themselves are being subjected to a morbid process. They no longer have the substance clearly stained, but it is turbid, even hyaline in appearance. The protoplasm too is considerably swollen, and its receptive quality to the aniline dye is no longer good.

The Virchow-Robin lymph space is entirely obliterated by the swelling, and in those portions of the structure where the tumefaction is most pronounced, there is also an almost complete obliteration of the His lymph space, the outer lamina of the vessel being closely pressed against the limiting lining of the peripheral edge of the perivascular space.

Changes in the adventitia are not nearly so distinct as in the two inner coats, though in places it holds considerable numbers of leucocytes, or these may be packed between it—in considerable numbers—and the outer wall of the lymph space. These white blood corpuscles are necrotic and swollen.

The contents of the perivascular space—where the degree of compression is insufficient to obliterate them—is interest-

ing and instructive. In them are large numbers of leucocytes in all stages of disintegration, and besides, there are frequently a number of protoplastic bodies, several times the size of a polynuclear leucocyte, very granular, and without nucleus, that are, probably, formed from the remains of the partially disintegrated lymphoid corpuscles that have aggregated into crescentic or ovoid shapes. Besides these partly organized bodies, there is a quantity of detritus, finely granular in character, insufficient to cause, without the aid of the lymphoid cells, any blocking of the lymph currents. Osmic acid produces a slight blackening of the degenerating white corpuscles, as well as of the detritus within the lymph spaces, showing that fatty changes are present.

The capillaries, like the intermediary vessels, are twisted and tortuous, the nuclei show changes similar to those in the larger vessels, while the cell bodies have departures from the normal in staining qualities, and here and there in the lumen are plugs of white blood corpuscles, which, from their closely packed appearance must have entirely stopped the circulation of the blood in these vessels before death. The lumen, beyond these plugs, is entirely devoid of contents.

Veins.—Changes in the coats of these vessels are similar to those in the arterial system, but aggregations of dying polynuclear corpuscles are more frequent, and are by far the most striking feature both of their contents and surroundings.

These aggregations, which in the small vessels, may vary from three or four to more than a dozen, are located both within and without the lumen. Within the lumen are collections of white blood cells filling the interior, while numbers are seen penetrating the walls. So vast are the collections in the perivenous spaces that the whole cavity is, occasionally, tightly filled, and the back pressure, from the plugs as well as the compression of the vessel from the outside, has attained such a height that in a number of instances the walls of the vessels have ruptured, and red corpuscles are intermingled with the white ones, and completely fill the His space. In one instance the site of the rupture was located in the section.

All the leucocytes, both within and without the veins show, with aniline stains, more or less evidence of disintegration, in some instances extending to complete destruction of the cell.

Arteries.—The medium-sized and larger arteries show individual differences as to the extent that they are affected by the morbid process. This difference would appear to depend largely upon the numbers of lymphoidal plugs in the arterioles and capillaries, for where they are thickly scattered, there the degree of arterial degeneration is greatest, and particularly is this true for the muscular layer. It would accordingly appear that at some period antedating the death of the animal, aggregations of leucocytes formed in the smallest vessels, and a slowly increasing backward pressure began within the arteries, insufficient to occasion complete stasis, but enough to create unusual pressure upon them; accordingly, this pressure in combination with the poisonous effects of the alcohol carried with the current of nutritive plasma, caused degeneration of the cellular elements forming the vascular walls, the main stress of the active process falling, upon the inner coats of the arteries.

This severely increased blood pressure is, probably, only an exaggeration of what ordinarily follows the administration of a moderate dose of spirits. Following its ingestion comes a dilatation of all the arteries of the body from the paralyzing effect of the drug upon the vaso-constrictor nerve fibres, and this endures for a variable time according to the quantity of alcohol partaken of.

The mechanism of the cerebral arteries—in that they do not possess vaso-constrictor nerves, but are dependent upon the inherent contractility of the muscularis and other elements—allows of a greater influx of the alcohol poison into the brain than elsewhere. The vascular muscular cells, under the influence of the direct action of the poison, and free from extraneous nerve influences to urge them to return to a normal state, remain for a long time inert, the congestion of the cerebral tissues is long continued, larger amounts of poisoned blood pass through the brain, and incidentally a larger proportion of alcohol than to other ordinary tissues, such as the muscles. As a result the deteriorated serum, laden with the poison is transuded in increasing quantities through the capillary walls; it is carried to the lymph spaces surrounding the principal cerebral cells, their structures are bathed in the diluted alcohol, their activity is dulled by its narcotic action and inertia and torpor of the functional activities are the result, and finally, it is only after the entire elimination of the poison from the system that they resume their normal functions.

If the amount of the poison to which the tissues are subjected is very considerable, as well as continued from day to day, and the excretory functions become clogged for a long time, the damage to the vascular walls is proportionally greater. In the light of the present experimental cases, the damage may proceed to necrotic changes in the endothelial lining and muscular layer. Leucocytes, formed in other portions of the body, mass in the cerebral vessels, from the increased quantity of blood brought by the arteries not being promptly carried off by the venous channels, and accordingly, we find a constant accumulation of the white corpuscular elements. This terminates, finally, in blocking of the capillaries as well as of the smaller veins, diapedesis, choking of the perivascular lymphatic channels, and eventual damage, both to the wall of the arteries by back pressure on a tissue already prone to undergo degenerative changes from the deleterious effects of a poisonous drug, and to the veins from abundant extravasations and transudations of the white corpuscular elements.

NERVE ELEMENTS.

Changes in the nerve cells, while definite to a certain degree, are by no means so intense as in the mesoblastic vascular structures. With aniline dyes positive degenerative changes are best determined in the neighborhood of the more extensively embolized vessels. Here the nerve cell bodies do not show the normal Nissl staining, but appear uniformly and

finely granular, also they do not take up nearly so much of the dye as cells that are located in areas in which damage to the blood-vessels is less severe. In the degenerated cells alterations in the nucleus and nucleolus are beginning, principally noticeable in the swollen and spongy state of the nucleolus, but the damage is not nearly so extensive or positive as in chronic alcoholism.

The silver-molybdate method shows more extensive changes than the Nissl, but these are confined entirely to the cell branches, which are invisible in preparations by the latter method. The departures from the normal in the dendritic extensions do not appear everywhere throughout the section, but like those noticeable in the aniline preparations are most definite where vascular damage is greatest.

The departure from the normal in the dendrites is shown by extensive and irregular swellings in the course of the branches extending over considerable distances in their long diameter, which suddenly decrease to the normal caliber of the stem. The majority of the lateral buds, or gemmulæ, are lost over the areas of tumefaction, though here and there damaged ones may be found projecting from the sides of the enlargment. Even the dendritic stems that have no swellings have a considerable diminution of the number of the lateral buds, and those that remain have lost a part of their natural characteristics, the rounded knob of the pear-shaped bud being lost, while the part that remains is seen as a short even projection from the sides of the protoplasmic stem. Often, also, those remaining have a greater thickness than is customary, from the insertion to the termination. Accordingly, it would appear that the remaining parts of the lateral buds were swollen. In places where the destructive process has been greatest, the gemmulæ are entirely stripped off from the parent branch.

So far as could be determined the axis-cylinder and its collaterals are not implicated in the destructive process.

Neuroglia.

With the aniline stains there is no increase of fixed nuclei among the tissues nor would this be expected in a semi-acute process. With the silver stain the supporting elements present no variations from the control. On the other hand the vascular neuroglia—belonging as it does to the lymph excretory system of the brain—gives distinct evidence that the stress of excreting a vastly increased amount of detritus from the rapid tissue changes present, as well as from working at a disadvantage under the narcotic influence of the alcohol contained in the nutrient serum, has been too much for its capacity. The cell bodies are larger, the protoplasmic extensions are thicker and more knotty, and the channeled arms extending to the perivascular spaces of neighboring blood-vessels are more prominent than in control preparations.

Conclusions.

1. In acute alcoholic poisoning, the stress of the action of the drug falls upon the tissues of the walls of the blood-vessels, rather than upon the nervous elements of the brain.

2. The involvement of the nerve elements is more gradual than that of the mesoblastic tissues, and only becomes noticeable, by present methods of staining and examination, after the lymphatic channels are choked with the detritus of white blood corpuscles and other cellular elements.

3. Nevertheless, the deteriorative action of ethyl alcohol on the nerve cell is apparent, and when prolonged, in more moderate doses than was administered to the rabbits, produces well defined cellular changes, as is evidenced by nuclear and dendritic changes.

4. In its action on the nervous tissues, ethyl alcohol may be likened to certain other poisons, such as ricin or the tox-albumins. The administration of these toxins causes the same departures from the normal in the nerve elements, but the alcohol has a much greater destructive effect upon the white blood cells, as well as the cells composing the walls of the blood-vessels.

5. The effect of the drug is proportionate to the quantity administered to the animal, as well as to the duration of its poisonous action before death ensues. Limited quantities continued over a considerable time accomplish, in modified form, the same destructive results as higher doses, acting during a few days.

THE ACQUIRED VENEREAL INFECTIONS IN CHILDREN.[1]

A Report of One Hundred and Eighty-Seven Children Treated in the Women's Venereal Department of the Johns Hopkins Hospital Dispensary.

"A STUDY."

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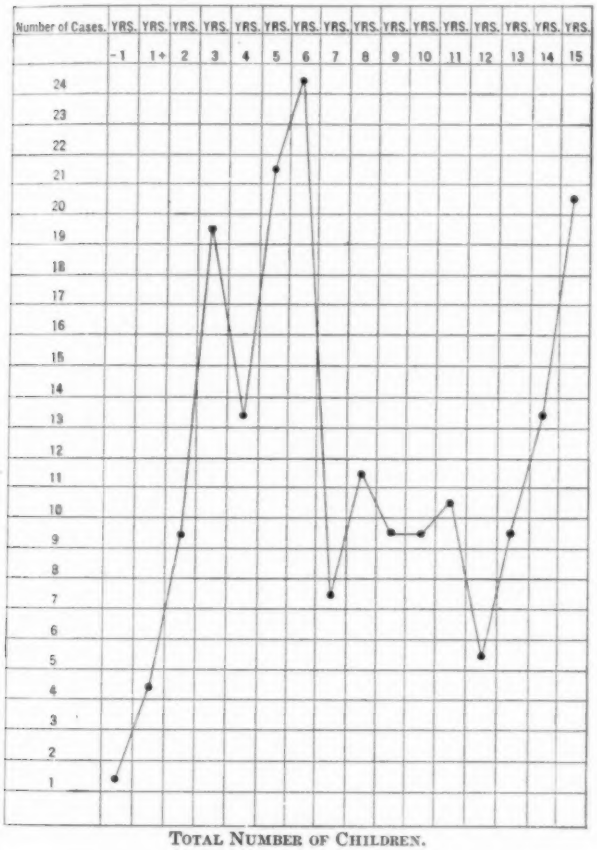
I

In a former report of the work of this department, I called attention to the unusually large number of young children brought here for the treatment of acquired venereal infections. This paper is a continued study of this phase of the subject with especial reference to its social, rather than its medical pathology, though for those interested in the medical side of it, I shall append the medical histories in brief of the cases, *ad seriatim;* referring to special cases only as they bear on certain points I wish to emphasize.

As I said before, and repeat with firmer conviction than

[1] Maryland Medical Journal, August, 1906. See also article by Dr. Abraham Wolbarst, J. Am. M. Ass., September 28, 1901.

ever, the cause of most of the outrages upon children is to be found in the superstition that a person infected with either syphilis or gonorrhœa may get rid of it by infecting another, and preferably "an untouched virgin." Thus a defenceless child is the most natural victim. This superstition is so deeply rooted in the belief of men that were you to ask ten police officers, cab drivers, hucksters, etc. of the truth of it I think eight would affirm it as a "*fact*," and all would know of its existence. Its basis, as I said in the former report, lies in the fact, that the syphilitic infected parents have no children



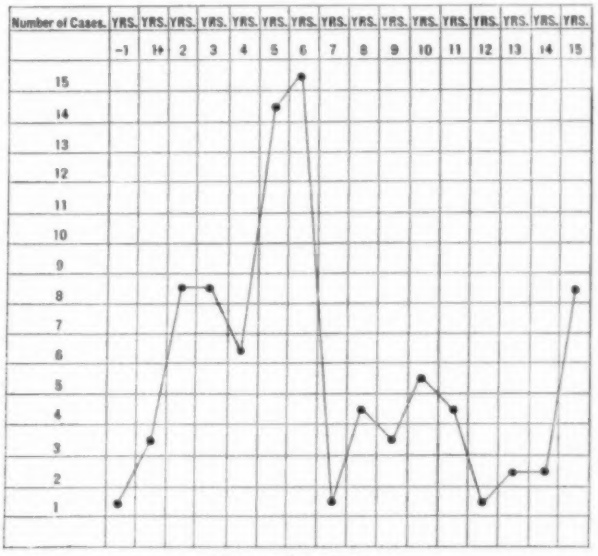
TOTAL NUMBER OF CHILDREN.

(except miscarriages and premature children, which in their ignorance they do not attribute to their disease), and when they do have a child, though it be diseased, they believe themselves to be healthy; they argue, that the child has taken the disease away from them, and therefore they are better, instead of recognizing the true explanation, that because they are better they have a child, "even though the child bears witness to their disease."

Time and again a woman has requested me to prepare her for maternity with the avowed intention of having, "the baby take the disease away from me"; again women, wise in this lore, tell other waiting women, that "they intend then to get rid of their disease," and the men patients admit that "they have gotten rid of their disease on a *baby*."

It is held by some that this abuse of infants and older children may be due to the form of perverted sexual instinct, known as Sadism, but the appalling number of these cases in this city (indeed in all more densely populated centers), about eight hundred to a thousand in a year, seems too large to credit to perverts; whereas the large number of physically diseased persons who wishing to rid themselves of their disease by infecting another, makes the "infectionist" theory, as I shall hereafter term it, more tenable.

In the charts which I have made of the ages of the infected children, it will be seen that far the greater number are six years and under, and of these the white children outnumber the colored, whereas after six, and when the sexual element begins to assert itself, the colored outnumber the white. There are fifty-four white children of six years and under, as compared with thirty-three colored, and sixty-three colored over six years of age, as compared with thirty-three white children over six years. On the other hand there is only one negro child between one and two years against one under a



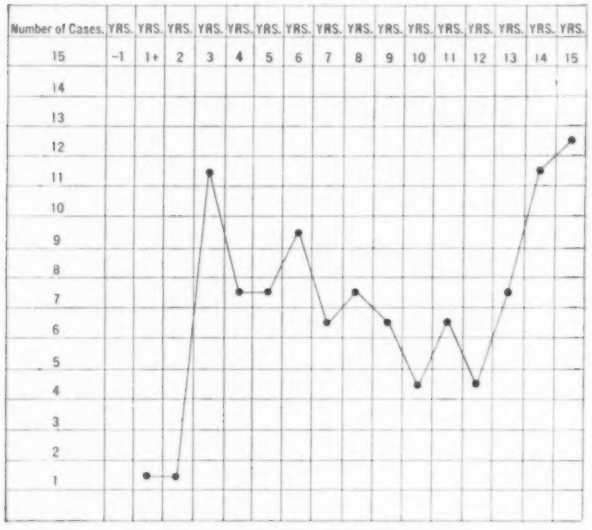
WHITE CHILDREN.

year, a ten-weeks-old white child (case No. 28, card No. 13,344), with hymen ruptured, a bubo, an ecchymotic spot on one labium, and a gonorrhœal vaginitis; one colored child at two years, three white children between one and two years, and eight at two, whereas the colored reach the maximum at three years with eleven cases, with only eight white cases at the same age, six at four, fourteen at five and fifteen at six years (see charts).

In studying the total number of both blacks and whites, we find the pitiful fact that there are almost as many children, nineteen in fact, of three years, as of fifteen years where there are twenty, or of five and six years where we find twenty-one and twenty respectively. These charts tell more eloquently

than words, the part the child plays in this tragedy since they were compiled to meet the charge so frequently made "that the children are vicious," a charge as cruel as it is stupid, since children at these early ages are not sexually vicious, that urges me on to the defence of babyhood, and girlhood in our city. It is not a fancied danger, nor an exaggerated condition that faces us, it is not only the child of the slums and of ignorant parents who is the victim, but every girl baby in the city (yes, even a boy) is in danger of infection, and the laity should know it and be warned. In my records I find the histories of two children, one of three and the other of three-and-a-half years, who had been abused; they are the children of well-to-do people, living in the best part of the city, and the records of other physicians record similar sad stories.

It is the hope of arousing intelligent interest in such a



COLORED CHILDREN.

state of affairs that this study is undertaken. The School Board of this city, at the instance of the committee on "Social Pathology of the Prisoners' Aid Association," has already agreed at its meeting of March 11, 1908, to exclude school children, reported to the chief truant officer, upon a reputable physician's certificate stating that the child ought not to attend school on account of an infectious disease, but not the nature of the disease; this step was taken because the Board of Health cannot, in the present state of public opinion, require the notification of these contagious diseases. If this is not done, infected children mingle with the uninfected, and thereby innocently endanger them; this is particularly true of syphilis, but it is a hardship to the child with gonorrhœa in that it goes to school when it should rest and be under treatment; that at least has been my experience.

The Juvenile Court also recently became interested and offered its co-operation, the presiding judge suggesting "that the court be notified of each case, and a probation officer be appointed to visit the child to discover, if possible, the guilty individual." The spontaneous sympathy and co-operation of these two bodies are a great encouragement in this work.

The police and detective departments of the city also have been helpful allies in the protection of these children.

The Juvenile Court has had three cases under its care and the Criminal Court will shortly determine the fate of a man accused by a fourth child, but in the vast majority of cases no clue to the perpetrator of the crime is ever obtained, often because of the youth of the little patient; at times through the unwillingness of the family to betray one of its members; and again, and perhaps oftenest, because the child has been attacked by a stranger or is too intimidated to tell what she knows; servants in the house not only endanger, but actually infect a child or children as witness the recent case of a six-year-old boy *viciously* infected by a nurse girl who was sentenced to seven years in the penitentiary. These infections are never accidental or innocent and this is the important point I wish to bring out in this paper.

It is usually easy to diagnose the case of an outraged child; such a child shows evidence of a ruptured hymen. However, it should be remembered that the child's hymen does not form when torn carunculæ myrtiformes, but simply serrations on its free border; it does not bleed freely because of its extreme delicacy of structure, resembling in this respect the lingual frenum, which as is well known is often cut and then torn for tongue-tie without loss of blood, or with only a few drops of a faintly blood-tinged serum. This is important in medico-legal cases, and it should be remembered also that in those children in whom the act has taken place more than once, the *hymen disappears entirely leaving the vagina an open canal continuous with the perineum,* without any evidences of carunculæ and NOT prolapsed as is a parturient canal after laceration. The ruptured child's hymen is characteristic and once seen is never forgotten.

In referring these cases to the acts of an infectionist rather than to those of a sadist, certain important differences are to be noted. The act of the infectionist is premeditated, is the result of a logical reasoning, and has no sensual, cruel impulse as its motive, but is always due to the belief that by infecting another, he purifies himself, whereas the sadist is a moral pervert, and seeks to gratify his sexual impulses, which are non-excitable in a normal manner, by a sensual gratification which is obtained through smell or sight or touch, and often without violence to the sexual organs of the victim. The infectionist wants primarily to get rid of his infection, and sexual gratification is not his guiding impulse. In proof of this is the fact that most of the children are infected with very little injury to the genital canal. I recall one case where a colored baby of two and a half years was brought to the dispensary by its mother almost immediately after the assault with no visible injury to the hymen or any other part of the genitalia,[2] and yet two days later the child developed a typical

[2] I had absolute proof that an assault had been committed!

gonorrhœa. As compared with this, is the case of a child of three who was cruelly torn by "the man's finger" as she insisted. She bled freely and the bloody hymen and vagina healed in five days without the development of gonorrhœa. This outrage was evidently committed by a sadist. The case is instructive from a medico-legal point of view, in that, with the marked laceration of the parts, the hymen healed with only the above-mentioned serrations, and with the left labium minus torn from its union at the posterior commissure as evidence of the attack. This injury to the labium resembles a peculiar congenital condition, and therefore may be misinterpreted by one unfamiliar with the facts of the case.

The infectionist wants "an untouched virgin," and therefore attacks children by preference, and the assault is always genital, and at times rectal also, as in a recent case, where a child of seven accused a man of two assaults, an accusation which seemed confirmed by the injury to the vagina as well as to the rectum; she has a gonorrhœa.

The sadist seeks an abnormal sexual gratification as described above, and attacks young and old, male and female, at times without regard to the sex of his victim, simply from a morbid impulse to gratify his appetite.

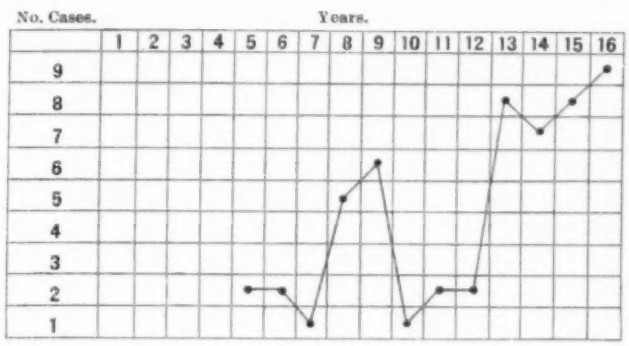
Many of the children admit that they have not struggled or cried out during the assault and the mothers assert that there was no blood on the child's clothes. The mother's first knowledge of the crime is derived from the the first purulent discharge she sees on the garments, when in many instances it is too late to discover the offender. These facts are opposed to the theory that the assaults are of a sadistic nature since all the evidence points to a normal sexual act.

I go into this detail because of the great difficulty in obtaining punishment for this crime. If it is a sadistic attack, and the offender a pervert, the law treats him as morally irresponsible. If the above theory of "infectionism" is correct, and I think closer study by others will prove it to be so, we may hope to get laws which will protect not only the child's honor, but also her health. As yet the laws to protect the honor of a female child are very lax.

In order to determine about how many of these cases occur in this city in a year, I visited the various station houses, and through the courtesy of the marshal had access to the records for a year, hoping to ascertain the number of cases of rape and indecent or felonious assault which came to the notice of the police. I took cases under sixteen years of age only, and although there were many, the very young children were not represented to the same extent as were the older, for the reason as I said before, that they are very often too young to tell or are too intimidated to do so (see chart below).

There were but sixty-one cases brought to the eight station houses in an entire year. Of fifty-two whose ages are given, the ages were as follows:

5 years.....	2 cases.	11 years.....	2 cases.
6 "	2 "	12 "	2 "
7 "	1 "	13 "	8 "
8 "	5 "	14 "	7 "
9 "	6 "	15 "	8 "
10 "	1 "	16 "	9 "



My own estimate of 800 to 1000 cases in a year in the entire city is based on the work done during the past six years in the Johns Hopkins Dispensary, where we see an annual average of about 30 cases. There are twenty other hospitals and dispensaries of which ten are teaching institutions in the city where such cases may be treated. In my estimates I use only the ten teaching hospitals, as I do not want to exaggerate the facts, preferring rather to underestimate them. If ten institutions treat each thirty cases in a year, they will treat altogether 300 children, and in Dr. Hooker's report 224 physicians reported 103 children treated for these infections in private practice in one year. If, therefore, 224 physicians treated 103 children in their private practice 1200 physicians would have treated about 550. Adding these to the dispensary and hospital total we get nearly 850 cases, an appalling number of infections of the most defenceless portion of the population. These estimates are low, and are so intentionally, lest exaggeration may be charged; unfortunately it is the real state of affairs, and it behooves us, medical men as well as laymen to arouse ourselves to the dangers of our little ones and to build a protecting wall around our defenceless children.

II

Analysis of Cases.

The acquired venereal diseases in children differ in no essential from those of the adult, save in two of the complications, *i. e.*, abscess of Bartholin's glands and pelvic abscess, the latter not occurring at all, the former rarely; and this is probably due to the undeveloped state of these organs in the child. Although pelvic peritonitis is rather common, it is of a low degree, and in this series of 189 cases has never reached the suppurative stage. The symptoms of peritonitis in a child, who has a gonorrhœal vaginitis or urethritis, are fever, abdominal tenderness usually with retraction, at times distention, vomiting and constipation. In nineteen cases or 10 per cent of this series, none of the children developed abscess. Although the child looks ill, it does not lie down, but throws itself over a chair lying on its abdomen, until the paroxysm is over (for the pain is paroxysmal), and then resumes its play; the child loses weight, is pale and fretful, but cannot be induced to remain quiet, proving that its condition is not as grave as in the adult. What the end result in these cases is, I have not yet been able to determine, *i. e.*, whether

or not the peritonitis interferes with the future development of the ovaries.

Bartholin's abscess occurred but three times or in 1.6 per cent; in cases No. 135, aged 14 (card No. 7750), No. 160 (card No. 88,386), aged 15, and No. 178, aged 9 (card No. 6236), the youngest in our series, who also had mastitis. Buboes on the other hand are rather frequent, twenty-eight or not quite 15 per cent developing large tender glands, though even here suppuration is rare, occurring but twice in the series.

Ophthalmia is as uncommon in the child as in the adult, occurring in case 77, aged 6, white (card No. 43,264), and in case 183, aged 8, colored (card No. 436), or two cases in 187. This is no doubt due to the lachrymal secretion of the adult eye, in contradistinction to its absence in the new born, as was pointed out in the report of this department's work two years ago.[1]

Arthritis is rare, occurring but three times, in case 18, aged 6 (card No. 8302), in case No. 105, aged 5 (card No. 70,672), who had peritonitis also, and case 149, aged 2½ (card No. 2982). One child, case 37, in this series, aged 10 (card No. 4660), had chorea, which cleared up under Fowler's solution; whether it was a complication of gonorrhœa or was independent of it, is difficult to say.

Involvement of the rectum is rather more frequent and occurs as a proctitis as well as an ischio-rectal abscess and occurred 7 times, about 4 per cent. Case 60, aged 1½ (card No. 25,589), had vaginitis with prolapse of the rectum. Case 75, colored, aged 7 (card No. 43,533), who had gonorrhœal vaginitis, with anal infection, had also lues. Case No. 82, white, aged 6 (card No. 45,254), had a bubo, vomiting, and recto-anal infection complicating the vaginitis. Case No. 87, white, aged 6 (card No. 39,535), had straining at stool, but as only one visit was paid to the dispensary, this may have been due simply to constipation. Case 88, colored, aged 3 (card No. 38,059), had rectal involvement. Case 146, white, aged 8 (card No. 2761), had enlarged inguinal glands and a proctitis. Case 159, colored, aged 11 (card No. 88,224), had a bubo, an ischio-rectal abscess and lues.

Seven cases had rectal complication though many children suffer from constipation and therefore many have blood in the stools; the cases referred to had definite gonorrhœal infections of the rectum.

Urethritis is the most frequent complication as would be expected occurring at all ages; thirty-six cases in all, or 18 per cent.

The double infection of syphilis, either as primary sores or as secondary lesions, and gonorrhœa occurred rather often. Taking the cases first that had primary sores there were 7, as follows:

Case No. 24 (card No. 10,914), colored, aged 13, primary sore with gonorrhœa.

Case No. 47 (card No. 16,029), colored, aged 5, primary sore with gonorrhœa.

Case No. 48 (card No. 14,756), white, aged 15, primary sore with gonorrhœa.

Case No. 114 (card No. 64,213), colored, aged 14, primary sore with gonorrhœa.

Case No. 119 (card No. 53,953), colored, aged 11, primary sore, then secondaries.

Case No. 172 (card No. 12,187), white, aged 9, primary sore with gonorrhœa.

Case No. 187 (card No. ——), white, aged 7, primary sore with gonorrhœa.

Of acquired secondary syphilis, but without absolute knowledge of the primary sore on the part of the physician, there were 29 cases—all colored children, varying in age from 3 to 15 years; 9 between the ages of 3 and 11.

Pregnancy complicated five cases, as follows:

Case No. 30, colored, aged 14 (card No. 558), lues also.

Case No. 45, white, aged 15 (card No. 16,405).

Case No. 64, colored, aged 13 (card No. 49,794), also luetic.

Case No. 135, colored, aged 14 (card No. 7750), Bartholin's abscess.

Case No. 140, colored, aged 15 (card No. 9839), lues.

It is interesting to note that all of the pregnant children had complications, either lues or Bartholin's abscess, and all had gonorrhœa. Bleeding occurred frequently, but it was of no importance except for the mothers' fears. It occurred sixteen times, twice preceding the gonorrhœal discharge, when it was doubtless due to the assault, and fourteen times during the gonorrhœal attack when it may be justly regarded as a complication, beginning from five to fifteen days after the onset of the disease, and continuing from a few days to two weeks; it is not very free as a rule, but enough to stain the garments or to show in the vessel after urinating. It is not always possible to locate the source, in case No. 185, E. G., aged 5 (card No. 28147), it came from the excessively hypertrophied caruncule myrtiformes which covered the entire surface of the hymen like a mass of granulation tissue. Of the cases that bled eleven were white, and only four colored; their ages ranged from two to ten.

One child had rhinitis; one a scarlatiniform rash over the entire trunk; one a cardiac lesion and peritonitis; one chorea; and one mastitis.

The extensive and very painful excoriations due to the gonorrhœal discharge must be regarded as one of the symptoms rather than a complication of the disease, as they are always present, even though proper treatment soon relieves the condition and if continued prevents its recurrence; it is a curious fact that in exacerbations of the disease redness is apt to occur with the discharge, when this is gleety, as well as when purulent.

The question of the contagiousness of the diseases is of the utmost importance, since the danger of other members of the family notably the children contracting it is very great. Syphilographers know that syphilis may be innocently contracted, but they are agreed also that gonorrhœa is almost always a venereal disease. The institutional epidemic gonorrhœal vaginitis may be pointed out as one of the rare exceptions. Let it be granted that these are not venereal in the true

[1] Maryland Medical Journal, August, 1906.

sense; but we must remember the curious fact, that all infectious diseases seem to gain in virulence in children's institutions, the mildest child's disease, "varicella" in the household, becoming a dreaded scourge in an institution; it may be therefore justly regarded, that these outbreaks in children's hospitals and asylums, are not in the same category with the subject under discussion, yet I would be skeptical even here, as the attendants are not all trained, educated people, and may accidently or even intentionally carry the infection from child to child.

From this standpoint I have collected the family infections, and find that in 189 cases five families with eleven persons were infected; there were three families with two children, and one family with three children as follows:

Case 97, G. R. (card No. 33127), aged 3, colored.
" 98, H. R. (" " 33124), " 7, "
" 148, M. D. (" " 2900), " 5, white.
" 149, R. D. (" " 2982), " 2½, "
" 151, M. L. (" " 3497), " 3, "
" 152, A. L. (" " 3498), " 6, } twin sisters.
" 189, C. L. (" " 65314), " 6, }
" 162, R. G. (" " 89801), " 5, white.
" 163, J. G. (" " 90021), " 2, "

In none of these cases could the source of infection be traced; in the family of three, the first case occurred early in the spring of 1906, and the two other children, one of the twins and the baby did not become infected until the following autumn, about six months later, and after the original one had been apparently well for months.

In one case in which an assault was attempted on two little sisters, the elder one awoke in time to escape the assault, and escaped infection, while the other little one less fortunate fell a victim to both assault and infection.

It must be remembered that at least two factors are requisite to infection, first an injury to the mucous membrane, and secondly a fresh living virus. If the mucous membrane remains intact, even the presence of virulent organisms will fail to produce infection, and on the other hand, an inert virus in an injured mucosa is non-infectious. The possibilities of towel, bathtub or toilet infections of gonorrhœa are extremely rare, but they offer a very useful shield for a guilty individual, and they also impede justice, and make it extremely difficult to protect children from these assaults. Let it be known once and for all that gonorrhœa is thus acquired only most exceptionally; and this possibility when offered in court as a defence should only be accepted after the most exhaustive examination of all the attending circumstances in the case. Gonorrhœa thus acquired probably occurs in much less than 1 per cent of all the cases.

TEMPERATURE.

The temperature in gonorrhœa without complications is not much above the normal, but any complication raises it considerably, though not for very long periods. The child with the cardiac complications is said to have had a temperature of 104° F., before admission, but on the day of admission it was 100° F., and never went above 102° F. A child who developed an ophthalmia had a temperature of 103° F. for a day only; another who had both a primary sore and gonorrhœa, developed a temperature of 103° F. when the secondary stage was ushered in seven weeks after her first visit to the dispensary; the child was very ill for several days but soon recovered her usual health and spirits, to have recurrences of her fever when treatment for the luetic infection was neglected. This case impresses upon me the necessity of the control of infected children, because it is now impossible to compel the parents to have the child properly treated or to keep her out of school during the infectious periods of the disease. This child was sent to school regardless of instructions to the contrary, and not only that, she was not brought back for treatment though the parents were urged and warned to do so.

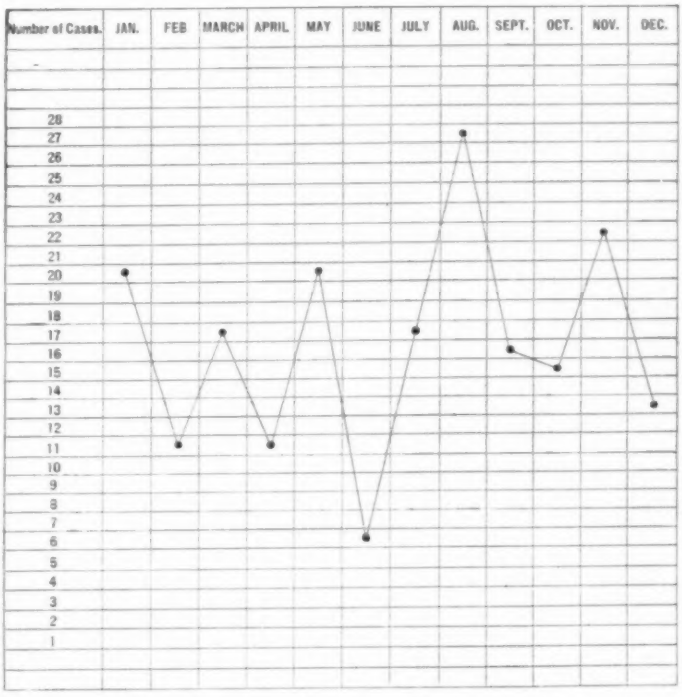


CHART SHOWING SEASONS OF INFECTIONS.

It is true our School Board, through its action of March 1, 1907, will co-operate with a physician to keep an infected child out of a school, but we *cannot compel the child to stay out,* if the *parents insist upon attendance at school*; therefore syphilis at any rate should be a notifiable disease for school children, and parents or guardians should be compelled to keep the children under medical care to insure the other children against infection when the child is returned to school.

Sanger, in his "History of Prostitution," calls attention to the influence of the heated season of the year as one of the factors in the crime of rape. To determine this point I have charted 196 cases and find that in the six cold months, January, February, March, October, November, and December, we have exactly the same number of cases as in April, May, June, July, August and September, 98 in both epochs. It is true

that in August there were 27 cases, the highest number of all, but it is equally true that in June we have the fewest number, only six, whereas January and May keep pace with each other, as do March and July; so that the cases which constitute the subject of study in this paper do not come under the heading of rape, but of infection, as a result of an individual trying to cure himself by becoming an infectionist.

It may be urged that it is not fair to draw conclusions from only 196 cases, but Kraft-Ebing calls attention to the increasing number of attacks on children in Europe and cites as one cause, this very superstition. The belief that sick people take the strength from the well, should they sleep together, is a very popular one to-day, among all classes of people; and the hope that the aged may gain vitality from the young is exemplified in the case of King David.[4]

Treatment.

Treatment as practiced in the adult seems to me of doubtful advantage; we cannot prevent complications, and we do not shorten the duration of the disease. All we can hope to do is to mitigate its severity. Some children come to the clinic but once; and we see recurrences as long as 18 months after the first manifestations.

One child, case No. 98, colored, aged 7 (card No. 33123), came with fresh signs every year in January, for three successive years, but I think this must certainly have been from repeated exposures, and not due to exacerbations of the original attack, such as occur in the cases above referred to, consequently treatment directed to the *cure* of *gonorrhœa* seems to me an almost hopeless undertaking, but treatment for the painful complications, such as the excoriations of the vulva and thighs, constipation, abscess and the like is very helpful. We usually treat the gonorrhœa with a 2 per cent protargol solution poured over the vestibule with a small glass syringe, and the reddened areas with zinc oxid ointment or a bismuth paste, one dram to the ounce; as a coating to the skin, to protect it from the discharge, and then to relieve the little sufferer, this is of great value. For the rectal condition, no local treatment is attempted unless there be an ischio-rectal abscess, which is incised and drained; the bowels are to be kept open, especially if peritonitis develops, and the child should be kept in bed, but this is almost impossible. Some writers speak of the extreme gravity of peritonitis in the child, but that has not been our experience. The case reported by Hunner and Harris in the Johns Hopkins Hospital Bulletin for June, 1902, and which ended fatally, was a patient in this department, but belongs to an earlier series of cases than those I report, and is the only grave case I have ever seen, and I think must be regarded as an exception. The vomiting of the little patients is easily controlled by small doses of calomel, 1/10 grain every half an hour, repeated five or six times, and very often a bland diet is all that is required with hot spice bags[5] to relieve the pain.

Bubos as a rule recede without breaking down, and although they may be so painful that the child limps, they seldom require treatment.

The arthritis in the few cases I have seen required no special treatment; either my cases so far have been exceptionally mild or grave inflammatory changes are uncommon in children. It is certain that so far none of the cases have required special treatment.

The syphilitic children receive the usual house specific, *i. e.*, bichloride of mercury and iodid of potash in solution graduated to their ages. They respond well as a rule, so well indeed that it is impossible to keep them under supervision in the absence of any legal control of this contagious disease.

The urethritis was not treated in any case, as the urethra is very small and the unfortunate children are so afraid of the pain, that no special local treatment is attempted, and only in some rare instances is the Lafayette mixture prescribed.

The only case of cystitis was irrigated with 1 to 5000 nitrate of silver solution and recovered after several exacerbations.

The other complications were treated as the case required, *e. g.*, one case of gonorrhœal vegetations was relieved, after the gonorrhœal discharge had ceased, by the actual cautery (Paquelin) under ether anæsthesia.

Summary.

The acquired venereal infections in children are far more common than the medical profession or the laity realize, and the increasing frequency of the infection of baby girls by criminal infection makes it a matter of the gravest concern to the social worker, the sanitarian and the legal protectors of the community.

Clinically the venereal infections in children run a milder course as regards grave complications, than is the rule in the adult, but the number of complications, and the duration of the disease seem almost identical.

The complications observed in the order of their frequency were:

Urethritis	36 cases.
Bubo	28 "
Secondary syphilis	29 "
Peritonitis	19 "
Bleeding	16[6] "
Primary sores	7 "
Proctitis	7 "
Pregnancy	6 "
Bartholinitis	3 "
Arthritis	3 "
Ophthalmia	3 "
Rhinitis	1[7] case.
Dermatitis	1[8] "
Chorea	1 "
Mastitis	1 "
Cystitis	1 "
Endocarditis	1 "
Gonorrhœal vegetation	1[9] "
Soft sore	1 "

[4] I Kings, Chapter 1. Death of King David.

[5] They consist of various finely powdered spices in a flannel bag, heated in whisky, their advantage being that they are light in weight and unirritating to the skin.

[6] Two before the development of gonorrhœa, fourteen after.

[7] The nasal discharge containing typical organisms.

[8] Scarlet rash.

[9] Case of venereal warts (probably gonorrhœal).

The duration of the disease as in the adult is variable, and cannot be prognosticated either by the intensity of the attack or the severity of the complications.

Sixty-seven or over 30 per cent made but one visit, the average of visits made was 3⅛, covering a period from three weeks to three years.

Treatment seems not to influence the course of the disease, the various methods tried to determine the relative merit of each were: Douching with potassium permanganate 1 to 5000, bichloride of mercury 1 to 8000, compound menthol powder used in the dispensary, silver nitrate solution 5 per cent strength applied directly to the vagina through a urethral speculum, and protargol 2 per cent in water or in glycerin poured over the vestibule only.

The treatment was given in the dispensary and supplemented at home by the mother; later we treated the child at the dispensary only, having the child come daily, or on alternate days, and finally at longer intervals, this too being supplemented by home treatment, but the results remained identical. As the little patients have been hurt before they come to us, they dread any attempt at treatment; and as all treatment directed to the vagina is painful, and cruel, since without beneficial results, I have for some time past used protargol simply poured over the vestibule, and the child soon learns that she is not to be hurt, and submits quietly, whereas under the former methods it required three people to hold and treat a six-year-old child, and the mothers had similar or more difficulty at home.

In protracted cases the child grows pale and thin, and for these the syrup of the iodid of iron or the elixir of iron, quinine and strychnine are beneficial.

The etiology of these cases is usually very evident. The hymen is either nicked in several places, presenting a characteristic serrated free border or it has one tear extending from the margin down to its vaginal attachment, usually somewhat to one or the other side, not directly in the median line. In medico-legal cases great stress is laid upon the fact that the mother did not see blood on the child's clothes. In the cases in which the hymen is not torn through, we can readily see why there was not much blood lost, not enough to stain the garments. The membrane is very thin and at its free border seems to be no more than the delicate mucosa, and tears without loss of blood just as the frænum of the tongue can be severed without loss of much blood.

In the secretion as it pours out of the vagina or urethra typical gonococci can readily be demonstrated, but not in that which covers the pudendum which does not stain at all or only feebly.

Prophylaxis seems to me the most important remedy for this condition. We must recognize the superstitions or perversions, call them what we may, and try to correct them by all the means in our power.

In Baltimore the various charitable organizations recognize the existing condition, and give lectures to spread the knowledge. The School Board co-operates with the medical profession to protect uninfected children by agreeing to allow an infected child to remain at home, simply on the strength of a reputable physician's certificate stating that the child should be kept at home. The Juvenile Court volunteered to co-operate with this department in bringing to justice the criminal or in protecting the child brought to its attention. The Police Department, and most important perhaps of all the State's Attorney's Office lends it aid in the prosecution of the "infectionists."

The Playground Association also takes much real interest in all conditions affecting the moral welfare of children, and to this end plans a course of instruction for the teachers and playground directors on this social evil. Many of the teachers in the public schools feel keenly the need of wider recognition of this crime on the part of the authorities, the parents and the public generally.

The Charity Organization Society of this city has inaugurated courses of lectures in colored church societies and meetings to teach the public the prevention and cure of tuberculosis as well as of this "the hidden plague"; it has been my privilege to address several of these meetings, and it is encouraging to feel that the knowledge and advice have not always fallen upon hostile or barren ground.

Of all the forces which have aided in encouraging me in this work none have done more in a practical way than the Prisoners' Aid Association of this city, for through it, the matter was brought to the attention of the School Board, and this Association stands to-day as the first organized non-medical body to recognize the gravity and importance of this condition, not only as it affects the school children, but all children and the criminal as well.

It may appear that the medical section of this study has not received the consideration it demands, but as curative treatment is so unsatisfactory we must direct our efforts to the prevention of the evil and that is indeed the object of this paper.

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CLEMENS von PIRQUET, Ph. B., M. D.

It gives us pleasure to announce that Dr. Clemens von Pirquet has been appointed Professor of Pediatrics in the Johns Hopkins University, and Physician-in-Chief to the Harriet Lane Home for Children, February, 1909. The hospital is to be erected on the grounds of the Johns Hopkins Hospital, and to be conducted in affiliation with the latter hospital.

It is expected that Dr. von Pirquet will assume the duties of the new chair in the autumn of 1909, and that the new hospital will be completed and in operation in the early part of 1910.

A few of the important dates in his life and the titles of his well known writings are given below.

Brief Sketch of Life.

Born May 12, 1874, at Hirschstetten, near Vienna.

Studied at University of Innsbruck and Louvain. Ph. B. (Louvain), 1894.

Studied medicine at Universities of Vienna, Königsberg and Graz. M. D. (Graz), 1900.

Graduate student at University of Berlin, 1901.

Assistant in Clinic for Diseases of Children (Professor Escherich, Director), University of Vienna, 1902-1909.

Habilitated as Privat-Docent, University of Vienna, 1908.

Principal Scientific Publications.

1. Zur Theorie der Inkubationszeit (The Theory of the Period of Incubation). 1903.

2. Die Serumkrankheiten (The Serum Diseases). (With Schick.) 1905.

3. Klinische Studien über Vaccination und Allergie (Clinical Studies on Vaccination and Allergy). 1907.

4. Die kutane Tuberkulinreaktion (The Cutaneous Tuberculin-Reaction). 1907.

Also a number of articles in medical journals and proceedings on subjects relating to bacteriology, infectious immunity and pediatrics.

LISTER PRIZE.

The Advisory Board of the Medical Faculty announces that the sum of $150 has been presented to the Medical Department by Dr. A. E. Malloch, of Hamilton, Ontario, with the request that it be given as a prize to the undergraduate student of the Medical School who shall write the best essay upon "Lister and His Work." The conditions governing the bestowal of the prize are as follows:

1. All essays in competition for the prize must be submitted to the Advisory Board through the Dean's office on or before February 1, 1910.

2. The Advisory Board will award the prize to the essay which in its judgment is most deserving, but it reserves the right to withhold the award in case none of the essays submitted are sufficiently meritorious.

W. H. Howell, Dean.

LAENNEC SOCIETY PRIZE.

A prize of one hundred dollars is offered by the Laennec Society for the Study of Tuberculosis of the Johns Hopkins Hospital for the best paper bearing on any subject relating to tuberculosis presented by a member of the Johns Hopkins University Faculty, or of the Hospital or Dispensary Staff, or any student of the University, or any independent investigator working in any clinic of the Hospital, or in any laboratory connected with the Hospital or University. The conditions of the prize are as follows:

1. All papers must be presented to Dr. W. H. Welch, chairman of the Award Committee, on or before March 1, 1910.

2. All papers must be typewritten and signed by some fictitious name, and must bear no mark to reveal the identity of the author. The paper should be accompanied by a sealed envelope bearing on the cover the fictitious name, and within the true name and address of the author.

3. Original work will be the basis of award, and careful clinical observation will receive as much consideration as laboratory experiments. Mere compilations from the literature will receive no recognition.

4. The paper receiving the prize will be read by the author at the meeting of the Laennec Society in April, 1910, and be published in the Bulletin of the Johns Hopkins Hospital.

5. The unsuccessful papers will be returned to their authors without delay, so that they may make other disposition of them.

6. The Committee of Award may withhold the prize if in their judgment none of the papers are worthy of it.

The three members of the Award Committee are: William H. Welch, M. D., William S. Thayer, M. D., J. M. T. Finney, M. D.

H. Barton Jacobs,
President the Laennec Society.

PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS MEDICAL SOCIETY.

January 4, 1909.

Dr. Frank R. Smith, the president, in the chair.

I. Case of Ichthyosis Hystrix. Dr. T. R. Boggs.

Dr. Boggs exhibited this lesion in a white woman of 52, who ascribed the condition to a birthmark due to a maternal impression. Her mother was frightened during pregnancy by a snake. Her belief is interesting in considering the peculiar snake-like character of the lesion.

The lesions were present from birth. They become very hard and thick, and turn black, every spring. The only pain present is from irritation of the clothing. In the summer the scales which have become a finger's breadth in thickness are shed.

There is no history of ichthyosis in other members of the family. The lesions consist of groups of slightly elevated papules covered by dense epithelial crusts which can be scaled off, leaving below them papillæ capped by apparently normal skin. There is no bleeding, soreness, or evidence of inflammation. The papules are distributed in a line along the anterior axillary fold, across the chest to the right breast, ending

at the midline. A similar fine line is seen along the median aspect of the right arm almost in the course of the brachial artery, extending down to the ulnar side of the wrist. There is a small group over the crest of the ilium and another in the right gluteal region. Extending to the popliteal space in the course of the sciatic nerve is a band, 2 cm. in width, of irregular rows of horny-crusted papules. They are continued on the anterior aspect from the knee to the ankle, and they are found upon the second and little toes where the crust of black, horn-like epidermis is particularly thick. Similar lesions are found along the outer edge of the foot and just below the external malleolus.

Dr. Boggs pointed out that the name ichthyosis hystrix means "porcupine" type of ichthyosis, so called from the large, horny outgrowth of the skin. The periodicity is characteristic. The patient sheds her skin when the serpents do. The distribution on the leg along the course of the sciatic nerve occurs in many cases.

Pathologically the lesion is a hyperplasia of the outer layers of the skin down to the mucous layer. An ingrowth or dipping down of the horny layer between the papillæ results in a compression and elongation of the latter. The black color in the spring is due to an increase in pigment—ichthyosis negricans.

The distribution in the course of nerves is only apparent. It is not substantiated by any nerve involvement. It is said to follow Voit's lines, the outer limits of cutaneous nerve distribution, also blood-vessels, and the lines of fissure in the skin, the lines of cleavage when torn. The lines of fœtal growth are mentioned. But none of the explanations cover all of the cases.

II. Investigations Concerning Rocky Mountain Fever. DR. H. T. RICKETTS, Chicago.

Dr. Ricketts exhibited maps showing the distribution of this disease in the Bitter Root Valley of western Wyoming, in Idaho, eastern Oregon, Utah, and Nevada. There is a small focus in Montana and Colorado. In the Bitter Root Valley it occurs on the west side only, a heavily wooded, mining and lumber district. The wood-tick concerned lives on the east side also, but is not liable to such contact with the residents on account of the openness of the country.

As to the disease itself, Wilson and Channing, in 1901, described a microparasite, a pyroplasma. They advanced the tick theory as reasonable for the intermediate host. They implicated the gopher because it comes out of hibernation at the time the ticks and the disease appear. Stiles studied the blood of patients and could not find the parasite. He also discredited the tick transmission.

The disease occurs only in the spring, from late in March to the middle of June in Montana. It is an acute infection with continued fever, enlarged spleen, and a characteristic eruption which is not unlike that in typhus fever. It begins on the wrists and legs. It is macular, but soon becomes nodular and indurated. It spreads over the entire body, the palms, soles, face, and back being included. It becomes hæmorrhagic and coalesces in a few days. The fever varies in height, 101° to 105° F., but is subnormal before death. The pulse is disproportionately slow, 80 to 90, becoming rapid in severe cases—a sign of bad prognosis. There is an early, general glandular enlargement. The cases generally recover.

On autopsy, the only feature is a large, firm, but friable spleen, richly cellular and moderately congested.

Dr. Ricketts began his investigations in 1906. He could not identify the organisms of Wilson and Channing. The inoculation of blood of diseased animals into guinea pigs caused a temperature of 105° and 106° F. after three days' incubation, and death after seven to ten days' illness. This was repeated in three instances. It is possible to infect a second and a third generation if blood is taken on the second day of fever. One hundred and fifty pigs have been inoculated from the same strain obtained in 1906. The pigs lose weight and show a cutaneous eruption similar to that seen in man. Hæmorrhagic slough of the scrotum and gangrene of the ears and the feet occur. In man gangrene occurs in those who recover, but is rare in Montana where the mortality is 75 to 95 per cent. It affects the scrotum, pharynx, and tonsils.

The transfer, of course, is of the virus in the blood, which causes a general infection.

Dr. MacCalla, of Boise, Idaho, found a tick on a human patient. He placed it upon a second person, with his consent, and the disease developed after an incubation period of seven to eight days. The patient recovered. This test was repeated with the same tick and the same result.

Dr. Ricketts made use of the predominating tick of the section; he allowed the female to feed upon an infected guinea pig, and then placed it upon a normal pig. A typical fever developed after seven to eight days of incubation. The pig recovered and later resisted infection, giving a positive immunity test. Other guinea pigs were infected from the same tick. The male tick can transmit the disease as well as the female. The larvæ and nymphæ can acquire the infection, retain it, and transmit it when in the adult stage. In fact, the disease is hereditary in the tick, a germ cell infection, which explains its continued existence from spring to spring.

Considering the source of infection for the ticks, he argued a priori that it must be some animal upon which it feeds. The foci upon the west side of the valley suggested an animal which is segregated and does not wander widely. Experimenting with wild animals he found the gopher, chipmonk, rock squirrel, and woodchuck were susceptible to infection from ticks. They are the hosts of the ticks, have habits of segregation, and meet all the requirements.

The prophylaxis is difficult in that the ticks are probably carried into the holes of these animals. This precludes their destruction.

As to immunity, one attack protects a guinea pig. The serum, however, has no striking curative effect.

Dr. Ricketts pointed out that the disease is not dissimilar to typhus fever. The latter is known to be transmitted by vermin.

The application of wild animals in studying this infectious disease suggests new reagents of which use is not being made.

Discussion.

Dr. W. H. Welch.—This is a most fascinating exposition of a new subject. These are model investigations. Professor Koch, on his recent visit, was very enthusiastic as to their value.

The possibility of working with typhus fever is most interesting. It is desirable to study typhus fever with this in view.

I should like to ask if it is similar to yellow fever in that the virus does not appear in the blood until just before death. Is there a cycle of development in the tick? Is the virus filtrable?

Dr. W. S. Thayer.—The mildness of the disease in Idaho is an argument against the disease being typhus fever. No epidemic of typhus fever has been as mild in large districts.

Dr. Ricketts, in reply.—The failure to transmit the disease from the guinea pig after death is probably due to the preponderance of immune bodies in the blood.

There is no cyclic development in the tick. The tick can infect in 24 to 48 hours, or as soon as it can be induced to feed again.

As yet the virus has not been readily filtrable. The work is not yet finished.

III. Study of a House Epidemic of Typhoid Fever. Mr. W. A. Baetjer.

Mr. Baetjer reported the results of his study of a small epidemic of typhoid fever, occurring in a colored family in the country north of Baltimore. Three of the members were admitted to the medical clinic during their attacks.

It was impossible to trace the source of the original infection as the first case died after a short, severe attack, and the rest of the family had no knowledge of her whereabouts prior to the onset. Typhoid fever occurs every autumn in this locality, however, and three years ago an epidemic of five cases occurred in the same house. This fact is of interest in that the whole region forms the northern boundary of the proposed reservoir for the city water supply.

In this recent epidemic nine cases occurred in house No. 1 and eight in house No. 2. The first case developed in house No. 1 in July. In August, after her death, her two children were attacked. Five days later, a husband, wife, and four children of another family in the same house contracted the disease. Nine of the ten people living in the house had typhoid fever, and two died. The diagnoses in these cases were confirmed by positive agglutination tests by Mr. Baetjer.

The water supply of the second house, one mile away, was a spring and a well, both of which were contaminated by drainage from both houses.

The first case, however, in the second household was a constant visitor to house No. 1, and probably received his infection by direct contact. In rapid succession seven members of the second family were taken ill.

Of the nine individuals not ill in this epidemic five had had typhoid fever previously. Out of 26 people, then, living in these two houses, 17 had typhoid fever. The infection in the subsequent 16 cases was due to direct contact with the first case. The source of the original infection could not be traced.

It is interesting that five of seven members of one branch of the family showed an enlargement of the thyroid gland—mother and four sons.

January 18, 1909.

Dr. Frank R. Smith, the president, in the chair.

I. An Experimental Study of the Metabolism and Pathology of Delayed Chloroform Poisoning. Dr. John Howland, New York.

Dr. Howland presented the results of metabolic and pathological studies in dogs poisoned by repeated or long chloroform inhalations. On the basis of percentage differences in the distribution of nitrogen as urea, ammonia, creatinin, or of sulphur in the urine, no distinction can be made on the day of poisoning between a dog that will recover and one that will die. The total nitrogen was increased in all cases. On the next day or two, the animals suffering late poisoning showed an increased output of creatinin, creatin, and sulphur.

Dr. Howland considered the intense destruction of body protein represented by these findings as the result of autolysis—a condition similar to phosphorus poisoning. Wells has pointed out that chloroform interferes with synthetic and oxidative processes without inhibiting autolytic processes. There was no increase in amino-acids and death was not due to an acid intoxication.

The pathological lesions found in these cases resemble strongly those reported in the fatal human cases. In both they are most severe in the liver and consist of central necrosis and fatty degeneration. The same may be said of the kidney lesions. In both there is also a tendency to hæmorrhage into the serous membranes and into the gastro-intestinal tract.

The experiments show that any prolonged anæsthesia with chloroform produces in the dog great alteration and even destruction in liver tissue. Dr. Howland believes that this is true of human beings as well as animals.

II. Ankylostomiasis. Dr. G. H. Whipple.

Dr. Whipple presented the results of his studies upon the presence of hookworms in 232 routine autopsy cases, performed in the Ancon Hospital, Canal Zone, Panama, in the year 1907-8. Hookworms were found in the intestinal tract of 72 cases (31 per cent), only two of which were *whites*. Because of the sanitary conditions upon the canal zone and the fact that most of the laborers wear shoes, Dr. Whipple felt the majority of the cases were infected in their native lands.

The old world hookworm was found in 39 cases (17 per cent); the new world hookworm, in 49 cases (21 per cent). The two were found together in the same case in 25 cases (11 per cent). The new world form predominated in all the heavy infections. In addition the presence of Trichuris trichiura was observed in 17 per cent of the cases and ascaris

lumbricoides in 8 per cent. One hundred and thirty-four cases or 58 per cent were free from intestinal parasites.

It was quite common to note hæmorrhages in the mucosa and submucosa (blood cysts) of the jejunum where the worm was attached or had been feeding. Large numbers of intestinal bacteria invade the mucosa with the worms and set up an extensive inflammation. Blood was found in the worms and Dr. Whipple felt that the worms could digest both red blood corpuscles and epithelial cells. He found worms in blood cysts which he judged from the inflammatory reaction were two to four days old. And these parasites were active and vigorous, and contained blood.

Contrary to Ashford, Baker, Yates, and others, Dr. Whipple does not believe the hæmolysin secreted by the worm is strong or can account for the anemia. As evidence is cited the very slight hæmolysis in a blood cyst of 0.5 cc. which has contained an active parasite for two to three days. The anemia is probably due to direct loss of blood and to the absorption from secondary foci of inflammation in the intestinal walls. The severity depends upon the number of worms and the intensity and extent of this diffuse inflammation.

February 1, 1909.

Dr. Frank R. Smith, the president, in the chair.

I. Surgical Cases. DR. J. C. BLOODGOOD.

Dr. Bloodgood reported a series of interesting surgical cases with the aid of the epidiascope and the pathological specimens. Among them was a muscular angioma of the cheek which contained a stone. The vein stone at one end of the tumor had been palpable for a number of years, and the condition had suggested sarcoma. Dr. Bloodgood cited the three cases reported by Dr. Davis in the Johns Hopkins Bulletin for March, 1908.

He exhibited the retroperitoneal glands and the spleen from a case of Hodgkins' disease, showing coagulative necrosis and metastases.

Lymphatic leukemia seldom gets into the surgeon's hands, but Dr. Bloodgood described a small boy with an acute attack of pain in the abdomen, nausea, and vomiting. More interesting was a uniform thickening of the gums as if they were infiltrated with salt solution. Sections showed lymphoid cells below the epidermis, and the circulating blood contained small mononuclear cells to the extent of 71 per cent of the total white blood corpuscles.

Somewhat similar is the condition of multiple myelomata. Dr. Bloodgood showed the skiagraph of a tumor in the outer third of the clavicle. There was no other lesion. This man had complained of pain in the shoulder. He was in good general health. The urine in this case contained the Bence-Jones body. And Dr. Bloodgood noted the importance of examining for this body in all cases of bone tumors.

Several cases of gastric ulcer were described, which disappeared after gastro-enterostomy. Similar relief was obtained in case of a duodenal ulcer. Excision was contraindicated on this account.

II. Fagopyrismus, with Report of a Case in Man. DR. HENRY LEE SMITH.

Dr. Smith said that fagopyrismus was derived from Latin *fagus*, beech-tree, and Greek *pyros*, wheat, and meant poisoning from the buckwheat. The condition is not uncommon in pigs, swine, horses, and such animals which eat the grains, plant, straw, or stubble of the buckwheat. White or spotted animals are especially susceptible, and the disease is moderated by shelter or a cloudy sky. It is attributed to fungi on the wheat or intestinal absorption from toxins generated by bacteria or by the sun's rays. An erythematous, itching rash occurs; a nervous type with mania; gangrenous dermatitis; hyperæmia of the brain. The treatment has been withdrawal of the poison, shelter from the sun, purgation, and cooling lotions. The condition clears up under treatment, but reappears in the sunlight. Death occasionally occurs from spasm of the larynx.

Dr. Smith's case was a man who was born in 1863. At the age of nine he ate his first buckwheat cakes at supper. He immediately felt as if there was hot lead in his throat and stomach. There was retching and vomiting. Hives appeared on the face. His eyes were bloodshot. He walked home, a distance of three miles, and was well the next morning. Later he experienced milder attacks and soon learned the cause.

He always experiences the burning sensation. Hives usually appear. And he has respiratory and gastric distress. Emetics relieve him, and recovery is a matter of a few hours. His skin desquamates for some time afterward.

He is on his guard constantly. Other cakes cooked on the same griddle are as poisonous. Pepper adulterated by buckwheat hulls has upset him. He can detect the adulteration by holding the substance under his tongue. Swelling, burning, and salivation make the test positive. Honey from bees which have fed on buckwheat has poisoned him, and a bag of buckwheat in the room caused violent sneezing even when its presence was unknown.

Dr. Thayer and Dr. Cole joined with Dr. Smith in putting the man through a series of tests.

As a cutaneous test, buckwheat was rubbed in a scarification upon the arm with white flour in a control. In a few minutes there were tightness in the chest, nausea, pain in the stomach, cough, a rapid, intermittent pulse, erythema, pruritus, and giddiness. The scarified area developed an urticarial eruption. On account of the irregularity of the heart, the arm was washed and in this way the control contaminated. Then a hive developed there also.

Later a similar procedure was followed, but no buckwheat used. There was no general disturbance. Buckwheat on a bench nearby caused no sneezing.

Finally different unknown powders were put upon the tongue. Many times he failed to detect the buckwheat, but finally gave a slight general reaction when the same buckwheat was employed as was rubbed in the arm.

Discussion.

Dr. W. S. Thayer.—This is a most remarkable picture! The immediate reaction to a slight scratch upon the arm was extraordinary!

Dr. Thayer described a case where from early childhood egg in any form by mouth caused similar symptoms. The life of the individual was made wretched because of the omnipresence of egg in foods.

Dr. Rufus Cole.—Dr. Cole considered this an anomaly in anaphylaxis. Usually hypersensitiveness is obtained by the giving of a small dose, followed by an interval, and then by a larger dose. It was conceivable to him that the patient was being repeatedly sensitized.

III. The Prophylactic Use of Hexamethylenamin in Cerebrospinal Meningitis. Dr. S. J. Crowe.

This paper was published in full in the Johns Hopkins Bulletin, April, 1909.

Discussion.

Dr. Harvey Cushing.—Dr. Crowe has not mentioned his experiments in vitro with the spinal fluid of patients. A patient was given urotropin and then specimens of spinal fluid taken every 15 minutes. These specimens showed graded amounts of urotropin, by color tests, and, when inoculated with organisms, gave graded amounts of organisms on cultivation.

Urotropin is important as a prophylactic measure, indicated in such operations with questionable technique as lumbar puncture, fracture of the skull, operations upon the nose, and in otitis media. Where complications are feared, urotropin produces an uncongenial medium for bacterial growth.

To illustrate the type of case in which urotropin proves a valuable measure, Dr. Cushing exhibited a man who had fallen from a travelling beam headlong on to his face in a mass of iron. The cranium was fractured through the ethmoidal bones, lacerating the right eye and cutting his lip. The seriousness of the injury lay in the fact that there was easy communication between the ethmoidal cells and the meninges. Surgical drainage was instituted and the patient put on urotropin within two hours after the injury. His recovery has been remarkable. There has not been a suggestion of bacterial infection.

This is a measure the eye and ear men will be very grateful for.

NOTES ON NEW BOOKS.

Clinical Diagnosis and Treatment of Disorders of the Bladder with Technique of Cystoscopy. By Follen Cabot, M. D., Professor of Genitourinary Diseases, Post-Graduate Medical School, New York. Illustrated. (*New York: E. B. Treat & Co., 1909.*) Price, $2.00.

This small volume has no marked characteristic to commend it; it is brief, but brevity in surgery is a dangerous quality oftentimes, and a doctor who means to practice genitourinary surgery should not depend on this work for his knowledge; he will do much better to read some of the more comprehensive text-books on the subject. It is doubtful whether the author's practice and advice is that of the best men in these lines to-day.

The Principles of Pathology. By J. George Adami, M. A., M. D., LL. D., F. R. S., Professor of Pathology in McGill University, etc. (*Lea & Febiger, 1908.*)

The fascinating style and the delightful personality of the author, which pervades this entire volume make it quite different from most text-books. The reader's attention becomes arrested without effort, and the interest remains throughout the many pages of theory which are usually so unattractive. The book is abreast with the times in one important particular, and this is the more to be commended since so far this field has not been dwelt upon in text-books on pathology. In the first section the cell forms the central point of interest, and after a histological discussion we are delighted to have the physiology and chemistry of the cell elaborated. There can be but little doubt that we have reached a period when the more intimate knowledge of the physiology and chemistry of the cell must form our means of attacking pathological problems. As the question of the origin of cells, though still remaining in absolute chaos, despite elaborate morphological studies, is on the eve of solution by the application of physiological and chemical methods, so we must agree with Adami that it is far better to prepare ourselves by beginning pathology as he has treated it than by the old method of studying any one system, like the circulatory system.

It was Adami himself who so brilliantly emphasized the evolution which sciences must perforce experience. The stage of hypothesis and wild theorizing, as he expresses it, leads to little good, and even though pathology may have reached maturity in some aspects, it is certainly far from being true that in its newer adaptations a like ripeness has been attained. And so the many theories, which we find in abundance throughout the work, do not help us much in the grasp of the known facts. These are still too meager, and the abundance of complex diagrams do not make a subject of such indefiniteness as enzyme action, growth, or even life, any clearer. How much the study of pathology will be facilitated by such a wide adaptation of the biophoric theory is yet to be seen.

Likewise, although interest does not lag, the relative importance of inheritance, heredity, and the theories concerning these, does not seem to warrant such a lengthy exposition as the author has given to them; nor do the well-known types of abnormalities and monstrosities seem to be deserving of such complete treatment. This becomes more evident since the chapter on bacteria as causes of disease is but brief, as is also the chapter on internal secretion. This latter is rather disappointing. In many places the author puts down still insufficiently confirmed work as facts. His theory that the distention of the vesicles of the thyroid gland may affect the vessels in the alveolar walls and their ability to absorb the contents of the alveoli seems rather fanciful. We do not feel sure from the unconfirmed results of Frankel that the corpus luteum plays such an important function as is indicated, nor do the anatomical and developmental properties of the islands of Langerhans seem to be absolutely settled. Later, in discussing transplantation of the thyroid, Adami says, "The animals die with symptoms of tetany, which follows extirpation of this gland in the cat." Of course this is only a slip of the pen, but it is one

which may greatly trouble the students. On the whole the treatment of the ductless glands and their secretions is very brief in consideration of the recent development of this subject. These deficiencies, however, are forgotten when we reach the chapter on inflammation and repair, which are treated in the same masterly style which has characterized his previous work on this subject. The chapter on immunity is of the same nature. Whether the student is more enlightened or more confused by the numerous and complex classifications of tumors is a question, but the interesting discussion of the predilection of various malignant tumors to metastasize in specific tissues is most suggestive and invites further study.

Briefly the way the author develops the subject seems the only rational way. The style is extremely attractive. There is far too much theory for the book to be of great use to the beginner in pathology. The student regards many of these theories as castles in air, and when he has finished with them has a vague idea of their value. In many places the conclusion drawn from these theories seems to be at fault. Still the scope of the book is broad. It is quite different from any other book which we have on pathology and will be of decided value to the student.

Green's Encyclopedia and Dictionary of Medicine and Surgery. Edited by J. W. BALLANTYNE, M. D., F. R. C. P. E. Vol. X. (*Chicago: W. T. Keener & Co., 1909.*) Price, $5.00.

Both the editor and the publishers are to be complimented on this work. The task of the editor has not been an easy one, but has been accomplished with skill and intelligence. The publishers have issued the Encyclopedia in an agreeable form, of good size and print. This is the last volume of the series, which is one that any doctor may be glad to own. With such a medical encyclopedia at hand, he is almost as well off as the ordinary person is with the British Encyclopedia. He will find it hard not to find what he wants. The judgment shown in the length of the articles is excellent, the more important subjects receiving their due space; and the information given is apparently quite up to date. In fact, this is a most useful and admirable reference work, and will prove of great help to any student of medicine.

Adenomyoma of the Uterus. By THOMAS STEPHEN CULLEN, Associate Professor of Gynecology in The Johns Hopkins University, and Associate in Gynecology in The Johns Hopkins Hospital. (*Philadelphia and London: W. B. Saunders Company, 1908.*)

In a beautifully illustrated and well-printed volume of 270 pages the author gives us practically all that is known of adenomyoma. During the last few years this subject has attracted wide attention, and been the theme of many dissertations, but among the many who have turned their attention to this subject, few have been as well qualified to treat of it as the author of this monograph.

In October, 1894, while making the routine examination of the surgical pathological material from the gynæcological clinic, Dr. Cullen found a uniformly enlarged uterus some four times the normal size. On section the increase was seen to be due to a diffuse myomatous thickening of the anterior uterine wall. As the condition appeared unusual sections were made of the entire thickness of the wall, which disclosed a diffuse myomatous tumor containing scattered bits of epithelium which apparently were continuous with the uterine mucosa. A few months later a second and similar tumor was met with, and a few months later still another. The first case was duly reported at the March meeting of the Johns Hopkins Hospital Medical Society in 1895, although the detailed report of the three cases unfortunately did not appear until the following year. Since then this subject has been of the greatest interest to the author, who has written extensively upon it, and his former monograph, which constituted the supplement to the Orth Festschrift in 1903, was based upon the study of 22 cases.

The present monograph is based upon the study of 73 cases of adenomyoma. These constituted 5.7% of the 1283 cases of myoma which came to the gynæcological laboratory of the Johns Hopkins Hospital between April 1, 1893, and July 1, 1906. Moreover, only the interstitial, subperitoneal, and submucous adenomyomata were considered in this percentage, and the smaller nodules which are quite frequently present in the cornua were purposely omitted from the routine examination. The above is of the greatest interest in showing that this tumor is far from a rarity, and yet the fact remains that it is accorded discussion in only a few of our recent standard text-books. The monograph is in reality a monument to the value of the routine examination of *all* pathological surgical material. We cannot refrain from calling attention to the fact that many of our recent and important discoveries have resulted from such routine work; witness the frequency of malignant degenerations of myoma, the many known facts concerning the futility of the older so-called radical operations for uterine carcinoma, the newer conception of the histological changes in the endometrium, etc. In the majority of institutions uterine myoma have been relegated to slop jars, or have been held of interest only on account of difficulties in the diagnosis or the surgical removal, and the subject of myoma has in general been regarded as closed.

The subject-matter is considered under the general headings of adenomyoma of the uterus, of the cervix, and of the uterine horn and round ligament. For clinical purposes the uterine growths are classed in three groupings, and thus considered, although it is clearly stated that mixed types may occur, as the types may merge imperceptibly from one to the other. The divisions of uterine adenomyoma are given as: 1. Adenomyoma, in which the uterus preserves relatively a normal contour. 2. Subperitoneal, and intraligamentary adenomyoma. 3. Submucous adenomyoma. These types are illustrated by the abstracted protocols of many cases, accompanied by descriptions of the growths which are pictured in their important features by many excellent drawings.

The author has paid especial attention to the etiology of this disease, and has grouped his cases with this view in mind in nearly all possible combinations. As a result of careful study of the cases reported in 1896, he concluded that the adenomatous elements of the tumor were derived from the glands of the endometrium in his three cases, thus differing from the theory which already had been advanced by von Recklinghausen, that usually they owed their origin to the remains of the Wolffian ducts. The case which von Recklinghausen took as the type rather resembled one of Cullen's earliest cases. v. Recklinghausen's tumor presented a peculiar glandular arrangement, in that in various areas several glands opened into a chief canal, which after passing a short distance became dilated, thus forming an ampulla. This appearance so strikingly resembled the microscopic remains of the Wolffian body, that von Recklinghausen concluded that the glands were derivatives of that structure in that case, in spite of the fact that the glands of the tumor reached the surface of the tumor in several places. v. Recklinghausen believed that the growth encroached upon the uterine cavity, caused partial atrophy of the mucosa, and thus allowed the glands of the tumor to open into the uterine cavity. He admitted, however, that the glands might be derived from those of the mucosa, and described another case in which he thought this was the case. As time went on, the majority of investigators favored the view of the derivation of the adenomatous elements from the remains of the Wolffian ducts. This phase of the subject, therefore, has long been of the keenest interest to Cullen, who has constantly studied his cases with this point in view. Serial sections have

been made from the various tumors until connection between the glands in the depths of the tumor and the mucosa could be proven, and in fifty-five or fifty-six cases of diffuse adenomyoma of the body of the uterus, was he able to demonstrate that the glandular elements of the tumor were derived at least in part from the uterine mucosa. The amount of work necessary to elucidate this point is apparent to any one who ever has worked in a laboratory. As earlier, Cullen believes that these glands are derivatives of the endometrium because they still retain their menstrual functions, as in nearly every instance in which cyst spaces are present, the cavities are partially or completely filled with blood, and even in the small and undilated glands blood is frequently present, or else the epithelial cells contain blood pigment—the remains of former hæmorrhage. This blood is held to be menstrual, and may present alterations in appearance just as does that in hæmatocolpos. The amount found in the cysts varies in accordance with the location of the cyst. It would be expected that the cysts in the uterine wall would attain only small size as they are constantly compressed by the muscle, and on the other hand when the cyst projects under the peritoneal surface, and are no longer so firmly compressed, they may dilate until they contain even several litres of chocolate-colored menstrual fluid. Moreover, typical uterine mucosa can be demonstrated in the solid portions of some parts of the tumor, not only by the appearance of the glands and the stroma on microscopic sections, but also because a typical conversion into decidual cells has been noted when the case has been complicated by pregnancy. The case recorded by Williams, in which the uterus of a woman dying two hours after labor was found to be the seat of a diffuse adenomyoma, the stroma of the glandular elements of which had been converted into typical areas of decidua, has been followed by a case described by Cullen. In this latter instance the case presented an unruptured tubal pregnancy of one side, and a subperitoneal adenomyoma of the other uterine horn. Here again the stroma of the adenomyoma had been in part converted into decidua, although the adenomyoma was at least 9 cm. away from the tubal pregnancy.

When we review the author's material from the standpoint of the origin of the glandular elements of the tumor, we find that in fifty-six of seventy-three cases of adenomyoma of all locations, viz., subperitoneal, submucous and interstitial, direct communication could be traced between the adenomatous elements and the uterine mucosa. Yet these figures are strengthened by the consideration of the tumors according to their various classifications. Thus some tumors were large and some were small. Moreover, few would demand that the continuity of the uterine mucosa into the depths of the tumor be shown in all classes of tumor in order to prove the origin as given, provided that the communication be proven in the interstitial and submucous forms, because we all believe that fibroids are usually interstitial in their earliest stages, and in their subsequent growth are displaced either inwards or outwards. In case the tumor developed outward, the continuity between the glands of the tumor and the uterus easily could be broken. As a matter of fact, there were eight cases of subperitoneal adenomyoma, and in no instance could the connection be demonstrated. There were seven cases of submucous growths. Some of these consisted in diffuse myomatous growths containing only a few small glands, while in others the glands had become cystic. In one case the myoma was fairly riddled with miniature uterine cavities which could easily be traced to the cavity of the uterus. There were fifty uncomplicated cases of diffuse adenomyoma of the uterus, some very extensive, others in the early stages. The uterine mucosa was traced into the myomatous tissue in all instances. In six other cases the adenomyoma was associated with squamous-cell carcinoma of the cervix, and in only one of them was there failure to show the continuity. There were two cases of diffuse adenomyoma of the body associated with adenocarcinoma of the body. In both cases the uterine mucosa had been converted into carcinomatous tissue, so that naturally the picture was so overshadowed by the cancer that the continuity of the glandular tissue could not be demonstrated. Thus, in only one of fifty-six cases in which the investigator expected to find that the glands of the tumor had developed from the mucosa, did he fail to do so. The above is quite sufficient to convince the majority of us that von Recklinghausen's theory cannot apply to a large proportion of cases.

The same general laws of the development of submucous or subperitoneal types of growth, holds alike for myoma and adenomyoma. As we have already indicated, the growths are interstitial at first and are displaced either inward or outward in their subsequent development. When they become subperitoneal, the glandular elements of the tumor gradually lose their continuity with those of the mucosa. This theory is well substantiated by the case reported by Lockstaedt, in which the development of a subperitoneal growth from an interstitial could be seen, and in which the mucosa could be seen extending deeply into the tumor.

From a survey of his cases the author concludes that at least in some instances, the myoma antedates the formation of the glandular elements: thus, he reports two cases and cites others from the literature in which a diffuse myomatous growth existed without an invasion of the glands. Other points bearing upon the etiology have been considered, although the cause for the development is still unknown. Contrary to the findings of W. A. Freund, Cullen has been unable to find that sterility or a previous infantile condition of the uterus was a prominent feature as an etiologic factor, inasmuch as only fifteen of forty-nine patients in whom the relation to pregnancy had been ascertained had never been pregnant, and of these six were unmarried. Nor would it appear that pregnancy with its incident stretching of the uterus leaves crevices into which the mucosa later could extend, as this explanation could not hold in the large proportion of cases that never had been pregnant. Of the forty-nine cases, thirty-two had had children, and two had had only miscarriages. The children averaged four to each one of thirty-one women in whom there was accurate records of the number of children born. In a few instances the woman had only one child, while in other cases there was a history of ten, eleven and thirteen children. Thus, it is found that the disease may exist in single, as well as in married women, and furthermore that it does not seem in any way to follow, nor yet to militate against normal pregnancy.

The age was investigated in 66 patients. The tumor was found in women as young as nineteen and as old as sixty, yet only five of the 66 patients were not between the ages of 30 and 60. Nearly one-third of the cases were found respectively in each decade between 30 and 40, 40 and 50, and 50 and 60. The development of the growth appears to be slow, as many patients dated the onset of symptoms five or ten years previous to the operation.

Forty-five cases were carefully examined to determine whether there was any causal relation between disease of the tubes and ovaries and the development of adenomyoma. None was found. Yet the interesting point was determined that in thirty cases there were more or less dense adhesions of the appendages on one or both sides. The adhesions were taken by the author to result from a mild degree of pelvic peritonitis, presumably caused by the diffuse myoma in most cases, although rarely other and more usual causes were found in the tubes. The pathological changes in the ovaries were such as are usually found in a corresponding number of abnormal adnexa examined in the laboratory routine. The uterus was found more or less adherent in twenty-four of forty-nine cases, showing the tendency of the tumor to form adhesions. The adhesions were usually confined to the

posterior surface of the organ and only rarely were noted on the anterior surface.

Adenocarcinoma of the corpus was found in two cases in which the cancer could be demonstrated as developing in the glandular substance of the tumor. One of these cases also strongly suggested the independent development of a sarcomatous growth of the body of the uterus. The co-existence of diffuse adenomyoma of the body and squamous-cell carcinoma of the cervix was noted in five instances. As would be expected, the symptoms of the latter naturally completely overshadowed those of the former, and the adenomyoma was not suspected until it was found in the post-operative routine examination of the uterus.

Three cases of adenomyoma of the round ligament are reported together with citation of other cases from the literature. The author believes that the glands in these cases are also derived from Muellerian tissues.

A resumé of the symptoms makes it appear possible the diagnosis can be made in many cases before operation. Cullen gives the following reasons for his belief: A case in which there is a diffuse uterine growth which is apparently a myoma can generally be diagnosed as an adenomyoma when, 1, there is a history of an ever-increasing menstrual discharge generally confined to the period; 2, dull aching or grinding pains during the periods in the uterus or down the back and thighs; 3, no intermenstrual discharge of any kind whatsoever; 4, curettage yields a rather thick but normal mucosa. As a rule no other pathological condition of the uterus gives this picture. The increased hæmorrhage is due to the participation of the mucosal structures of the tumor in the menstrual function, and the pain is due to the retention of the blood in the glandular spaces, and the subsequent dilatation of the latter.

On account of the diffuse nature of the growth as well as the great frequency of pelvic adhesions this disease cannot well be treated by myomectomy, and supravaginal hysterectomy is advocated. The author shares the general belief that adenomyomata are benign and cites a case in which a woman from whom a wedge-shaped portion of the growth was removed in 1895, remained well and free from symptoms during the space of eleven years, and was so up to the time of the publication of the book. That incomplete myomectomy is not always so successful in the cure of symptoms is shown by another case which was not relieved until later subjected to hysterectomy. There was, however, no development of malignancy.

The volume is a faithful record of an investigation which has extended over the long period of thirteen years. The amount of work essential to the elucidation of this subject has been absolutely enormous, and is scarcely hinted at in the text. Nor will one be able to appreciate the extent of such a labor who has not done the routine work of a large laboratory. The volume is everywhere characterized by systematic and careful work, and although a monograph, an unnecessarily large portion of the text is not consumed by the history of cases, which are presented only as abstracts and to illustrate the salient features. The illustrations are beautiful and for the most part are the work of Horn and Becker, although the wonderful drawings of Broedel, which illustrated the earlier papers of Cullen on this subject, are included. The illustrations present the novel feature of being tinted instead of the more usual black color. To our mind this is a pleasing and agreeable departure. The publishers have presented a most attractive volume, well printed in large and clear type, and handsomely bound, which makes the whole a delight to the eye.

In conclusion we congratulate the author upon presenting to the scientific world another monograph worthy of his reputation and the school.

FRANK W. LYNCH.

Contributions to the Physiological Theory of Tuberculosis. By CHARLES CREIGHTON, M. D., Sometime Demonstrator of Anatomy, Cambridge Medical School, Etc. Price, 12/6. (*London: Williams & Norgate, 1908.*)

The text, consisting of 238 pages, is divided into three parts.

Part I. Histogenesis of Experimental Tubercle.

The author gives a summary of previous researches on Histogenesis. Referring to the advent of cellular pathology he says: "Incidentally the cellular pathology involved a separation of true tubercle, as an interstitial connective-tissue neoplasm, from the infiltrations, exudations, etc., both caseous and gelatinous, which Laennec had included along with the miliary nodules. The distinction has not been made good, etc." (p. 3).

Baumgarten's theory of the histogenesis of tubercle is contrasted with that of Metschnikoff; the former holding that the bacilli stimulate the fixed connective-tissue cells and endothelial cells of the blood-vessels to change into epithelioid cells in which the bacilli are found and which may increase in size and contain two or three nuclei.

Metchnikoff's theory is that the small granular polynuclear leucocytes first gather the bacilli and engulf them. After a few days these cells are destroyed and large mononuclear cells, which meanwhile have arrived on the scene, absorb the detritus of the polynuclear cells and the bodies of the bacilli, and from this two-fold pabulum grow to be epithelioid cells, and some to giant cells.

The author also reviews those studies of the blood in connection with the histogenesis of tubercle, and then takes up what he calls the "Select Experiment-Species," *i. e.*, the rabbit and guinea pig. These animals have been used because they are convenient rodents and because of the certainty and rapidity of their infection with pure cultures of tubercle bacilli.

Peculiarities of the blood are stated to exist in these animals and stress is laid on the presence of glycogen in the tissues.

The following criticism of the use of the guinea pig is rather surprising: "If human or bovine tuberculous tissues should happen to have few or no bacilli, or from any reason to be ineffective for inoculation purposes, a sure way to make the argument from them go is to inoculate in a guinea-pig, and to use its spleen. But does anyone know the natural capabilities of the guinea pig's spleen as infective material? Is there an unusually powerful ferment in its pulp for the reduction of red blood corpuscles? What is the meaning of its histological peculiarities in the fœtus, in ordinary, and in pregnancy? Usage has brought this organ into a position of great importance in the logic of experimental tubercle, and yet its natural properties are little known, and are assumed to be negligible" (p. 27).

The author proceeds to a discussion of the histogenesis of tubercle in various organs of the rabbit and guinea pig, using a considerable amount of his own material and drawing extensively on the literature for evidence corroborative of his views, often interpreting the findings of other observers in a very different way from their interpretation of the same. It is a somewhat difficult task to pick out from the great mass of citations which are interjected throughout the entire text, the author's own views.

The following quotations, some of them rather widely separated in the text, and not set down here in the order in which they occur, perhaps summarize the author's views: "The primary effect, and sole direct effect, of the bacilli is upon the red blood corpuscles" (p. 57, under discussion of "the spleen of the tuberculized rodent"). To this altered state of the blood the author ascribes certain other changes in the histogenesis of tubercle. "As to the endothelium of blood-vessels, my attention was called to it first in studying the meningeal arteries of tuberculous children, from which one gets the impression very strongly that the endothelium must have been softened or rendered glutinous, or

otherwise altered, by the quality of the blood constantly passing over it, so that blood-discs stuck to it, penetrated amongst its cells, and even collected in heaps between it and the elastic lamina. But in the pulmonary veins at large in the tuberculized rabbit one may find proof positive that the endothelial lining has been acted on by the blood passing over it" (pp. 38 and 39).

It will be seen later that the above observations are very significant of the author's theory of the histogenesis of tubercle.

I digress just a moment to make one observation. If the changes in the endothelium of the veins are due to the quality of the blood constantly passing over it, one would expect the same changes to be produced on the endothelium of the arteries, but the author declares in his account of the effect in the lungs of intravenous inoculation in the rabbit, "One finds the arterial endothelium normal" (p. 39).

Composition of a Tubercle.—"The bulk of the tubercle is a protoplasmic tissue, trabecular or syncytial or plasmodial, with large nuclei usually vesicular and clear. This is the distinctive tissue of all rodent tubercle, whether in the lungs, lymph-glands, spleen, kidney or liver" (pp. 42 and 43). This characteristic tissue is, as I understand it, nothing other than the epithelioid cells of other authors.

Now the first *evident* change in the formation of tubercle the author believes to be thrombosis. This thrombosis leads to diapedesis of red blood corpuscles. The extravasated blood is broken down under the influence of a ferment which the author derives from certain pre-existing cells. In case of the lungs, "the karyokinesis of the leucocytes (as well as of the alveolar epithelium) is in relation with the dissolution of the red blood corpuscles" (p. 29).

In this connection the author refers to an earlier paper in which he "illustrated the disruption of the hæmatoblasts on the inner wall of a sero-sanguineous cyst of the dog's neck to yield red blood corpuscles" (p. 29). The phenomenon which he there described was the disruption of the nucleus of certain cells connected with the detachment of pieces of the outer or protoplasmic zone to become red blood corpuscles. Applying this observation to the formation of the epithelioid cells of the tubercle he says: "What I have now to urge is, that the same fragmentation of nuclear chromatin, and the same clinging of the nuclear particles to red blood corpuscles, is found in the building up of the large mononuclear protoplasmic cells in rodent tubercle: they are built up from the substance of blood-discs by the action of nuclear chromatin (e. g., of a leucocyte) where the blood is thrombosed within the vessels or extravasated into the air cells, ... the one process being an assimilation of blood-discs (or their substance) to make large protoplasmic (epithelioid) cells, the other being a dissolution of the protoplasm of large epithelial-like perivascular cells to yield the blood-discs: the karyokinesis is the same in both, but the end is reversed" (pp. 29 and 30).

The epithelioid cell being the peculiar and characteristic element of the tubercle it is of interest to see how the author derives it in the various organs of the body.

In the lungs he believes that they are probably derived from the alveolar epithelium.

With reference to their origin in the liver the author says: "In the larger portal branches from which the thrombus has been dislodged, the endothelial cells are greatly thickened, with large and highly chromatic nuclei and with blood-granules in their protoplasm, the original mosaic pavement being still recognizable. So far as my observations go, I would not make the liver-cells contributories to the tubercle" (p. 54).

In the spleen the pulp-cells are the elements which eventually develop into epithelioids. "The variety of appearances is such that it is hardly possibly to generalize them, otherwise than to say that the pulp-cells are becoming epithelioid cells by reducing and assimilating the substance of red blood corpuscles" (p. 58).

In the description of the histogenesis of lymph-gland tubercle it is not perfectly clear what the origin of the epithelioid cell is; "large multinuclear or giant-cells are rare, elongated or spindle-cells are common, but commonest of all are the epithelioid cells, with enormous nuclei, which may be joined by their ends to form the kind of syncytium already described for the lung and spleen. In very fine sections it is still possible to see a certain relation of this tissue to the walls of the capillaries" (pp. 60 and 61).

To trace the author's views of the histogenesis of the giant-cell would be even more difficult than has been the task of arriving at the origin of the epithelioid cell. The following from page 44, under histogenesis of the tubercle in the lungs of the rabbit, indicates one theory of their formation advanced by the author: "Some part of the thrombus may become a giant-cell; and the reason why the bacilli are found most usually within giant-cells is that the latter are intravascular formations, or thrombi organized in a peculiar way."

In Part I, Histogenesis of Experimental Tubercle, the author makes a primary injury to the red blood corpuscles the essential underlying principle in the histogenesis of tubercle. This injury to the red blood corpuscles enables them to be broken down under the influence of the ferment-like action of certain cells, and the resulting products furnish the pabulum on which these cells develop into the component elements of tubercle.

The author does not assume the presence of the bacilli at the site of the tubercle to be always an essential, as evidenced by the following: "Inasmuch as tubercle bacilli are few or altogether wanting in all forms of liver tubercle, whether spontaneous or experimental, excepting where masses of them had been thrown direct into the portal blood, we may conclude that the noxious agent need not be actually bacterial, but some substance which doubtless arises from bacteria in the experimental case, and is able to coagulate the portal blood, not from its excess in that region, but because the blood in the portal vein is peculiarly susceptible" (pp. 51 and 52).

In Part II, Placental Analogies of the Rodent Tubercular Neoplasm, reviewing the results described in Part I of injecting tubercle bacilli into the venous blood of rabbits, the author states that the ultimate textural result in the lungs, liver, spleen and lymph-glands (all organs of blood renewal) is the same in all, "namely, a rich protoplasmic nucleated tissue, which has been called plasmodial not inaptly, and is often a true syncytium from the fusion of several nuclear territories, being a peculiarly rodent neoplasm" (p. 62).

In this Part the author proposes to show "that a similar plasmodial or syncytial tissue is built up, also from the substance of reduced red corpuscles, in the placenta—notably similar in the two rodent species, but not different in kind in the chorionic villi of the human placenta; . . . . that the indeciduata have a peculiar provision, on the amniotic and allantoic surfaces, for the deposit of hyalin and caseous waste from the fœtal blood, which represents a part of the placenta of the deciduata, and is an equally good analogy for the dead matters of tubercle; . . . . That the process of caseation in rodent tubercle is just the same as in the rodent placenta (guinea pigs)."

I shall not attempt to follow the author through the complexities of his "Placental Analogies." To do this successfully, much more to attempt any critical review of the evidence submitted, would require a histologist well versed in embryology and pathology.

In the section VIII, "Present State of the Argument from Experiment," one is surprised to find this statement, "Amongst the hundreds of papers of the last ten years, ... it is hardly possible to find one which does not assume that human tubercle is an infection, and that the bacillus of Koch is the infective agent. It is a wonderful unanimity on the nature of a great disease—a disease almost damned in a fair theory. Yet the doc-

trine of a specific bacillary cause has been all the while in a state of flux; it has been modified by its author; and if it be scrutinized closely as it now stands, it will be found to be beset with difficulties and paradoxes" (p. 120).

Referring to the lesions produced by the butter bacillus, the hay bacillus and others, he says: "The way out of the labyrinth is to follow the clue of histogenesis in each particular case, and to drop all idea of conformity or nonconformity to an absolute structural type, as if there were any such due to any bacillus" (p. 127).

In the light of the "Placental Analogies" it is hard to see how histogenesis will lead out of the labyrinth; indeed, one almost wonders if it is possible to differentiate, by histogenesis, a case of miliary tuberculosis from a normal pregnancy.

In Part III, Human and Bovine Tuberculosis, the point of view from which the author approaches the pathogenesis of bovine and human tubercle is as follows: "Nearly the whole of bovine tubercle is a chronic disorder of nutrition, to which breeding may predispose in a very high degree. A large part of human tubercle is also chronic and a disorder of nutrition, to which also breeding predisposes greatly. For the acute cases of practice, especially in children, there may be analogies among the experiments; but they are far more likely to be found in the experiments with complex proteids ("tissue fibrinogens") than in those with bacteria. Infants and children must often receive as food complex proteids—for example, in the milk of anemic cows—which are absorbed undigested into the portal blood or the lacteal lymph, and may even produce extensive portal thrombosis, or, at all events by their cumulative action, a state of the blood which favors minute multiple thromboses of the meningeal arterioles, of the terminal pulmonary arteries, of the interlobular veins of the liver, of the splenic arterioles, etc.

"No experiments on the smaller mammals can ever reproduce the manifold circumstances of human and bovine tubercle; but the results of the experiments as they have impressed the whole profession, so ought they to be analyzed critically to find their points of agreement with the tuberculosis of experience. It is then seen that there is nothing specifically infective common to the two, but only such a histogenetic process as was to be looked for in the respective circumstances, the physiological analogy for it being found in the neoplasm by which the nutrition of the fœtus in the utero is carried on at the expense of the reduced red corpuscles of the mother" (pp. 134 and 135).

It would be of interest to know the author's views on the histogenesis of cancer and sarcoma. What is the "pabulum" on which the cells feed to produce the malignant neoplasm, and if this, too, is reduced to red blood corpuscles, what is the primary agent which so injures the blood that it may be dissolved to form this "pabulum"?

In Part III the author discusses human and bovine tuberculosis, all the cases referred to being described as "spontaneous tubercle"—a term apparently used in contradistinction to tuberculosis experimentally produced.

He then considers in order, lymph gland tuberculosis, with reference to lymph glands in syphilis, tumor cases, etc., the formation of hyalin in tuberculous lymph glands, bovine pearl-disease, its physiology and the occurrence of mast-cells in it, the occurrence of similar structures on the serous surfaces of human beings, which led the author in an earlier paper to advocate the theory of the transmission of the bovine disease to man; and meningeal, splenic, hepatic, pulmonary, and internal tubercle as arising spontaneously in man and bovines.

Throughout this section the same phenomena of thrombosis and dissolutions of the red blood-cells to furnish the pabulum of cells which go to form the tubercle are observed.

An interesting observation is that on hæmoptysis in pulmonary tuberculosis. "The blood brought up in the beginning of phthisis is often so unattended with signs of violent reaction, being sometimes even without the incitement of coughing, that there is every reason to look for its source in passive congestion of the mucous membrane of the bronchi.

"Nothing has occurred in the subsequent study to affect the original conclusion that hæmoptysis, in the great majority of cases, comes from an unbroken, passively congested mucous membrane, and only in occasional instances (usually fatal at once) from a ruptured small aneurysm of the pulmonary artery or from the eroded end of an artery (a rare thing) in a cavity" (pp. 230 and 231).

The author evidently does not consider hæmoptysis to be due to the presence of tubercles, but to the cause which led to the formation of tubercles, namely, an antedcedent venous stasis.

I have not attempted a critical review of the author's work, for which I frankly confess my incompetence, but have sought rather a descriptive account. The text is fully illustrated with drawings which are pertinent and clearly explained.

The author displays a wonderful knowledge of the literature of the subject which he brings into relation to his own views, often interpreting the results of others in a different way from that in which they did.

The style is very difficult, owing to the frequent interruption of the narrative by parentheses and citations from other authors. There is scarcely a paragraph which does not contain one or more parentheses or citations, and often both.

The language in places is fantastic, but the humorous similes are apt and furnish momentary relaxation from the strain of trying to follow the intricacies of the subject, for which the reader is grateful.

The author is a severe critic of those whose work he has noticed, and early in the book he enters upon a lengthy and caustic criticism of the Histological Report of the Royal Commission on Tuberculosis (the present British Commission), which does not seem wholly relevant, even if just.

W. L. Moss.

BOOKS RECEIVED.

Scientific Memoirs, No. 35 (New Series). By Officers of the Medical and Sanitary Departments of the Government of India. *Black-water Fever.* By Captain S. R. Christophers, M. B., I. M. S., and Dr. C. A. Bentley. 1908. Fol. 239 pages. Government Monotype Press, Simla, India.

The Baby. A Book for Mothers and Nurses. By Daniel Rollins Brown, A. B., M. D. 1908. 12mo. 200 pages. Whitcomb & Barrows, Boston.

Diseases of the Digestive Canal. (Œsophagus, Stomach, Intestines.) By Dr. Paul Cohnheim. From the second German edition. Edited and translated by Dudley Fulton, M. D. [1909.] 8vo. 373 pages. J. B. Lippincott Company, Philadelphia and London.

American Practice of Surgery. A Complete System of the Science and Art of Surgery, by Representative Surgeons of the United States and Canada. Editors: Joseph D. Bryant, M. D., LL. D.; Albert H. Buck, M. D. Complete in Eight Volumes. Profusely Illustrated. Volume Five. 1908. 4to. 965 pages. William Wood and Company, New York.

Mind and Its Disorders. By W. H. B. Stoddart, M. D., F. R. C. P. With Illustrations. 1909. 8vo. 488 pages. P. Blakiston's Son & Co., Philadelphia.

Orthopedic Surgery. By Henry Ling Taylor, M. D., assisted by Charles Ogilvy, M. D., and Fred H. Albee, M. D. With two hundred and fifty-four illustrations. 1909. 8vo. 503 pages. D. Appleton and Company.

Text-Book of Diseases of the Nose, Throat, and Ear. By Francis R. Packard, M. D. [1909.] 8vo. 369 pages. J. B. Lippincott Company, Philadelphia and London.

Retinitis Pigmentosa, with an Analysis of Seventeen Cases Occurring in Deaf-Mutes. By William T. Shoemaker, M. D. Laboratory Examinations of the Blood and Urine by John M. Swan, M. D. With illustrations and three colored plates. [1909.] 8vo. 106 pages. J. B. Lippincott Company, Philadelphia.

Text-Book of Gynecological Diagnosis. By Dr. Georg Winter, with the Collaboration of Dr. Carl Ruge. Edited by John G. Clark, M. D. After the third revised German edition. Illustrated by four full page plates and three hundred and forty-six text illustrations in black and colors. [1909.] 4to. 670 pages. J. B. Lippincott Company, Philadelphia and London.

Surgical Diseases of the Abdomen. With Special Reference to Diagnosis. By Richard Douglas, M. D. Second edition, revised and enlarged. Edited by Richard A. Barr, B. A., M. D. Illustrated by twenty full page plates. 1909. 8vo. 897 pages. P. Blakiston's Son & Co., Philadelphia.

Illustrations of the Gross Morbid Anatomy of the Brain in the Insane. A Selection of Seventy-five Plates Showing the Pathological Conditions Found in Post-Mortem Examinations of the Brain in Mental Diseases. By I. W. Blackburn, M. D. 1908. 4to. 154 pages. Government Printing Office, Washington.

Experimental Researches on Specific Therapeutics. By Prof. Paul Ehrlich, M. D., D. Sc. Oxon. The Harben Lectures for 1907 of the Royal Institute of Public Health. 1909. 16mo. 95 pages. Paul B. Hoeber, New York.

Bacterial Food Poisoning. A Concise Exposition of the Etiology, Bacteriology, Pathology, Symptomatology, Prophylaxis, and Treatment of So-called Ptomaine Poisoning. By Prof. Dr. A. Dieudonné. Translated and edited, with additions, by Dr. Charles Frederick Bolduan. Authorized translation. 1909. 8vo. 128 pages. E. B. Treat & Company, New York.

Blood Examination in Surgical Diagnosis. A Practical Study of its Scope and Technic. By Ira S. Wile, M. S., M. D. 1908. 12mo. 161 pages. Surgery Publishing Company, New York.

Seven Hundred Surgical Suggestions. Practical Brevities in Diagnosis and Treatment. By Walter M. Brickner, B. S., M. D., Eli Moschcowitz, A. B., M. D., and Harold M. Hays, M. A., M. D. Third Series. 1909. 16mo. 150 pages. Surgery Publishing Company, New York.

Studies in Puncture-Fluids. A Contribution to Clinical Pathology. By. O. C. Gruner, M. B., London. 1908. 8vo. 289 pages. P. Blakiston's Son & Co., Philadelphia.

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